UNIV. OF
TORONTO
LIBRARY

Digitized by the Internet Archive
in 2010 with funding from
University of Toronto

http://www.archive.org/details/proceedings1901newy

N E W Y O R K

P A T H O L O G I C A L

S O C I E T Y

P R O C E E D I N G S

N E W S E R I E S

V O L. I 1901-02

211310
13.4.27

Published by the Society

New York

RB
1
N32
U.S.
v.1

Proceedings

of the

New York Pathological Society.

NEW SERIES, Vol. I. February, 1901. No. I.

TABLE OF CONTENTS.

BROOKS, The Occurrence of the Bacillus Aërogenes Capsulatus in the Human Body.—GOLDHORN, A New and Rapid Method of Staining the Chromatin of the Malarial Organism.—EWING, Remarks on the Origin of "Colloid Carcinoma of the Peritoneum."—HODENPYL, Endothelioma of the Breast; A Specimen of Cystic Kidney.—SCHULTZE, Ruptured Aneurism of the Basilar Artery; Sacculated Aneurism of the Middle Cerebral Artery.—LEWALD, Tuberculous Appendix; Two Congenital Cysts of the Kidney; Two Cases of Large Uterine Fibro-Myomata Complicated by Pregnancy.—THAYER, Specimens of Hypertrophied Prostate.

DR. EDWARD K. DUNHAM, *President.*

THE OCCURRENCE OF THE BACILLUS AËROGENES CAPSULATUS IN THE HUMAN BODY.

*Abstract.**

HARLOW BROOKS, M.D.

Cases of infection with the bacillus aërogenes capsulatus have been very carefully studied and there is little more to be investigated concerning the biology and pathology of this bacillus, as the work of Welch and Nuttal, Welch and Flexner, Dunham, Norris, Fraenkel, and others has exhausted these fields of research. What seems still to be an important line along which work may be directed, is the determination of the habitat of the bacillus and its occurrence in the human

* This paper will appear in full in *The Journal of Experimental Medicine.*

body. For us, these conditions as present in New York City are of especial interest.

In twenty-five consecutive autopsies performed at the city morgue, on bodies not over twenty-four and less than forty-eight hours dead, seven were noted which showed rapid post-mortem decomposition with visceral and subcutaneous emphysema, a condition almost invariably due to the bacillus aërogenes capsulatus.

Ante-mortem infections are less frequent, but statistics are difficult to obtain, as comparatively few cases are reported, and the hospitals do not keep accurate records concerning this point. Surgeons say that the cases are not infrequent, and the atria are usually found in wounds which have been soiled with dirt or fæces.

A systematic search was recently made for the bacillus aërogenes capsulatus in the organs of the body to which the recorded cases seemed to point as the chief sources of infection. The methods employed were as follows: the material which was obtained from the cases was at once transferred to tubes of ordinary bouillon or of bouillon which contained one per cent. of glucose. These tubes were sealed with melted paraffin, after the paraffin-anaërobic method of Park, and were then placed in the incubator at a temperature of 38 degrees C. After the cultures had been in the incubator from twelve to twenty-four hours, all those tubes in which gas had formed were found with the paraffin disk forced up for a greater or less distance from the surface of the fluid, which was fairly frothy from gas production. Cover-glasses of this growth were then examined, and if a bacillus morphologically similar to the bacillus aërogenes capsulatus were present, the whole contents of the culture-tube, about 10 c.c., was slowly injected into an ear vein of a rabbit. Three to five minutes later the animal was killed, usually by forcing a small quantity of air into the perforated ear vein, or sometimes by chloroform. The carcass of the rabbit was allowed to remain at a temperature of from 28 to 30 degrees for from five to twelve hours, when it

was examined for subcutaneous and visceral emphysema. If this were absent the experiment was recorded as a negative result. When it was present to a slight degree and when there was any reasonable doubt as to the presence of the organism, cultures from the blood, liver, and subdermal serum were made and were subsequently examined for the bacillus aerogenes capsulatus. Where typical "Schaum-organe" were present, as was usually the case, except in those instances which were wholly negative, smears of the liver were examined, and if they showed the presence of a large number of bacilli morphologically like the gas bacillus, positive to Gram, and usually encapsulated, the experiment was recorded as positive. In the first experiments, cultures also were made in these doubtful cases, and the bacillus was more accurately identified by hanging drop for non-motility, and by sporulation on blood-serum, after the method of Dunham. A few were also isolated in pure culture, but it was finally decided that the demonstration of subcutaneous and visceral emphysema in the animal, with the presence of numerous bacilli morphologically similar to the bacillus aerogenes capsulatus in the cover-glass smears was sufficient to identify the bacillus. Welch and Flexner also seem to consider this diagnostic. At the first thought these methods seem crude and inaccurate, but experience has proven them to be quite reliable.

The discarding of an original culture and recording a negative result in case of failure of gas production will probably be attacked, for it has been stated that the bacillus may grow without the formation of gas. This statement does not seem to be warranted, though the amount of gas formed varies much. By utilizing the paraffin-anaerobic method of Park, gas, even in minute quantities, can be detected. For some time, however, the cultures in which no gas was produced were examined both in cover-glass preparations and by injecting the culture into rabbits, always with negative results.

The production of marked visceral and subcutaneous emphysema in the rabbit seems quite diagnostic, though later

another organism is mentioned which may produce the same lesions though in a less degree; but smears from the liver were always sufficient to exclude the organism.

Occurrence of the Bacillus Aerogenes Capsulatus in the Soil.

The bacillus has never been isolated from the soil around New York, in so far as the author is aware; and as the season was not favorable no investigations were made by me. When, among the few cases reported, the large proportion in which the infection took place from dirt coming in contact with fresh wounds is considered, it would seem evident that the soil around us is thickly inhabited by this gas-producing bacillus.

Occurrence in the Intestine.

The first series of cultures to determine the presence of the bacilli in the intestinal tract were from the recta of cadavers in the city morgue. These bodies were taken consecutively as they came to the tables, omitting all those which showed any marked evidences of post-mortem decomposition. The age of these bodies varied from three to forty-eight hours after death; all had been kept in excellent cold storage.

Half the cultures were obtained by separating the skin from the anus and introducing a sterile glass rod for a distance of 5 cm.; the other half were gotten by opening the lower half of the sigmoid flexure and rubbing the glass rod against the mucous membrane; as the results were identical, they are classed together. Twelve cases were examined in this manner, and from the cultures of eleven the bacillus aerogenes capsulatus was obtained. The single failure was from the corpse of a child two months old where a member of the colon group alone was found.

In a similar manner cultures were made from the recta (per anum) of six healthy soldiers, and in four of these the gas bacillus was found. The inoculation material taken in these instances was purposely small; in one of the negative cases

movements of the bowels were obtained by daily enema, which may possibly have cleansed the mucosa of the bacillus.

Occurrence in the Male Urethra.

The male urethra of the cadaver was examined in only two cases; in both care was taken to exclude possible outside infection, but the material secured was collected fully 7 cm. within the urethra. Both cultures showed the gas bacillus in great abundance.

Cultures were made from the normal urethra in ten surgical cases which gave no history of previous urethral disease. The material for inoculation was secured by introducing a small platinum loop about 5 cm. into the urethra, the lips of the meatus first being carefully everted. The amount of material so obtained was very small, but of the ten cultures three contained the gas bacillus.

Occurrence in the Female Genital Tract.

Abundant cultures from the upper portion of the vagina of three cadavers showed the presence of the bacillus in all.

Cultures made from collections of mucus posterior to the cervix in six gynæcological patients showed the bacillus aërogenes capsulatus in two. Naturally it is difficult to obtain cultures from the normal vagina, but all cultures were taken before the cases were examined and represented the condition usually found in dispensary practice.

Occurrence in the Nasal Cavities.

The presence of the bacillus in the dust presupposes its existence in the nasal cavities, and cultures from the noses of four normal men showed the bacillus in one. All the cultures from the nasal cavities showed much gas when they were grown in ordinary bouillon; as this condition was also present in many of the cultures from the throat, this variation will be considered under that heading.

Occurrence in the Throat.

But one authentic case of infection of the bacillus aerogenes

capsulatus through lesions of the throat was found, and that is Case I. of Dunham's series, where the infection was preceded by a severe ulcerative tonsillitis. It is quite possible that at least some of the cases of Ludwig's angina are really infections of this nature.

Cultures were taken from the throat, in the region of the tonsils, either direct from the surface of the tonsil or from collections of mucus, above or below, between the pillars. Thirteen cases were so examined, none of which showed the presence of the gas bacillus.

When the bouillon cultures from the throats were placed under anaerobic conditions, there was a profuse formation of gas in the tubes, from nearly every case. This gas was devoid of foul odor, and neither the bacillus aerogenes capsulatus nor any other bacillus resembling it were found in any of the cultures. Cover-glass preparations showed a bacillus about the size of colon bacillus, with rounded ends and oval shape. When these cultures were introduced into the circulation of a rabbit and the animal killed from three to five minutes later, quite an extensive visceral emphysema was produced, especially marked in the liver and kidney. Subcutaneous emphysema was present in these animals in a lesser degree than when the gas bacillus was the infectious agent, but the condition simulated that produced by the bacillus aerogenes very closely. Smears of the emphysematous organs showed that the bacillus was occasionally encapsulated. This organism was not fully identified, but it probably belongs to the bacillus mucosus capsulatus group.

When these experiments are considered, it must be remembered that one bacteriological culture taken from a large surface, such as that of the vagina or nasal cavity, when negative, means nothing, and from this series of examinations it would seem that, as a matter of fact, the bacillus aërogenes capsulatus is always, or nearly always, present in the tracts considered. In dealing with them we must so regard it, and it is to be hoped that this small investigation will help to em-

phasize the great importance of thorough antisepsis or asepsis in dealing with these important tracts, even in minor operations and procedures. Doubtless the bacillus exists in the soil, dust, and fæces, frequently at least in a sporulating form, and as such it is particularly resistant, sometimes surviving a temperature of 99 degrees for one minute (Dunham).

The histories and autopsies of four cases were reported, three which showed that the infection had probably taken place from the intestinal tract, and one where the origin might have been the posterior urethra or dirt infection of skin lacerations caused by direct traumatism.

In the greater number of cases "gas infection" seems to take place immediately before death and spreads very rapidly in extravasated blood and blood clot. This is a strong surgical argument for thoroughly evacuating clots when possible, especially when they are in proximity to the pelvic or perineal structures, where these infections are most likely to occur.

In one case a bacteriological examination of a frothy pus from a tumor of the groin showed the presence of bacillus aerogenes capsulatus. The cavity was immediately treated surgically, and after the patient's death, a month later (apparently from pulmonary tuberculosis), no bacillus aerogenes capsulatus could be found at autopsy.

This shows that much may be done in the way of treatment, if the case is immediately diagnosticated.

A NEW AND RAPID METHOD OF STAINING THE CHROMATIN OF THE MALARIAL ORGANISM; ALSO A REPORT ON CHANGES OBSERVED IN ERYTHROCYTES CONTAINING SUCH PARASITES.

L. B. GOLDHORN, M.D.

The staining of the chromatin of the malarial organism has hitherto been a rather difficult undertaking. Romanowsky, Gautier, and Zieman obtained their results by accurate mixtures of certain brands of methylene blue and eosin. Manna-

berg used hæmatoxylin and picric acid after first extracting the hæmoglobin from the red corpuscles. Nocht's discovery that polychrome methylene blue contained a body staining the chromatin of the organism was important, and his method is now the one in general use; but an accurate mixture of his neutral polychrome solution and eosin is required in order to obtain the coveted result. All the above methods require long fixation, certain brands of methylene blue, prolonged staining; and the final mixture must be made just before using.

The method I have worked out is a very simple one and gives superior results; moreover, it shows a cell degeneration which, so far as I can determine, has not been recorded.

My *modus operandi* is as follows: A fresh and thin blood-smear is fixed for fifteen seconds in pure methylic alcohol or in peroxylic spirits. This short fixation is amply sufficient, and it appears to be preferable to other fixing methods in vogue, when it is a question of staining by my method. The fixed smear is washed in running water and stained for seven or more seconds in a $\frac{1}{10}$ to $\frac{1}{5}$ per cent. aq. solution of eosin. Any kind of eosin may be used, though I give Grubler's yellowish *wasserloestich* the preference. Wash again and stain for ten seconds in a faintly alkaline polychrome methylene blue solution which has been prepared as follows: Dissolve two grams of methylene blue in 300 c.c. of water. No special brand is needed. Shake the solution well and add four grams lithium carbonate; shake again thoroughly and pour into a large open porcelain dish over a water-bath. Allow the boiling water to touch the bottom of the dish. Stir frequently and decant, after fifteen minutes, into a glass-stoppered bottle. Filter paper should be avoided; and cotton may be used in the funnel. Set aside for a few days and slightly acidify with a four per cent. or five per cent. solution of acetic acid. Now add enough of a saturated aqueous solution of lithium carbonate to render the stain faintly alkaline. In order to know when this point has been reached, trial blood smears should be stained, as suggested, until the addition of another trace of

lithium carbonate solution causes the red cells to take on some of the blue. With some practice this point is rapidly determined. A stain prepared in this manner does not deteriorate; on the contrary, it seems to improve on keeping if kept in well stoppered bottles. By diluting the stain several times, after correcting the reaction, one obtains a much more manageable solution than if it is used full strength. To determine the best time of staining, a number of smears should be left in the dye for a varying number of seconds, and the interval giving the desired result fixed upon.

The preparations exhibited this evening were prepared by this method; but the polychrome solution used in staining them was not always prepared as stated. An old solution of Unna's alkaline methylene blue which has been kept until methyl red has been formed gives fine chromatin staining, but the degeneration of the infested red cells does not appear to be so clearly revealed as with a dye which contains a good deal of unchanged methylene blue; nor is ordinary basophilic degeneration of erythrocytes well seen.

So far as the preparation of the stain goes, I think that lithium carbonate gives better results than potassium carbonate. Sodium or potassium hydrate were failures in my hands, and the solution of polychrome methylene blue (Grübler) in the market did not give the desired result.

By heating for only fifteen minutes considerable methylene blue remains unchanged; and the advantage of this will be seen presently. Filtering through filter paper is avoided because a good deal of valuable staining material is lost by absorption.

The dyed preparation should be dried, after the last washing, by rapid agitation of the cover-glass or slide. Heat is sometimes harmful. Filter paper should not be used for drying.

By this method of staining, certain peculiar granular degenerations of the malarial infected blood corpuscles were observed. Erythrocytes containing the very young forms of

parasites contain granules which are distinctly basophilic to dyes. As the parasite grows, and the hæmoglobin diminishes, the staining characteristics of the granules become altered and appear in successfully stained preparations as distinct, reddish granules. The appearance of these infected cells is so singular that one unfamiliar with the dye would scarcely suspect them to be remnants of erythrocytes, framework or skeleton alone remaining.

Why do these granules stain bluish at first and reddish when the parasite is reaching maturity?

How much do they have in common with the ordinary granular degeneration of erythrocytes, such as has been observed, by Dr. Grawitz of Berlin and by his assistant, Dr. Hamel, in cases of lead poisoning, malaria, progressive pernicious anæmia, and in certain septic diseases?

With the staining method that I have described in this paper it may be observed that certain megaloblasts in pernicious anæmia possess a closely granular cytoplasm, whilst other megaloblasts may have but few granules, some of which may be quite coarse. Some, on the other hand, may be wholly devoid of granules.

The nucleus of megaloblasts stains beautifully by this method. An intranuclear network is well shown. Necrosis and polychromatophilia may be observed. Other nucleated red cells stain well; and polymorphonuclear neutrophiles show their granules and chromatin-bridges. Lymphocytes stained for a short time frequently show nucleoli in a thick capsule, and basophilic granules in the cytoplasm. Lymphocytes may be stained deeply; hence the stain is a desirable one in lymphatic leukæmia. Blood platelets show purplish dots within a bluish body.

No matter how little corpuscle substance may be left around a segmenting body in tertian fever, it will always be plainly seen as a granular network at the periphery; and thus it may be demonstrated that intracorpuscular segmentation is rather the rule than the exception. The chromatin of the young

forms of the malarial parasite stains readily, and an achromatic zone (or is it an achromatic substance?) remains unstained.

I believe that the term ringform is a misnomer, and that the parasite is never a true ring. The achromatic portion plays an important rôle in the splitting up of the chromatin. It does not seem to disappear completely at any time.

By varying the staining method somewhat one may frequently observe a peculiar network in the red cells. Whether this is an artifact or not I cannot say.

It will, of course, be very interesting to try the method on the blood of birds and frogs containing parasitic organisms. I have, thus far, been unable to obtain fresh specimens of such blood.

In order to obtain chromatin staining, correction of a polychrome dye is not a *sine qua non*.*

To Dr. Dunham I am indebted for many valuable suggestions. Had it not been for the facilities extended to me by him I should have been unable to work out the method.

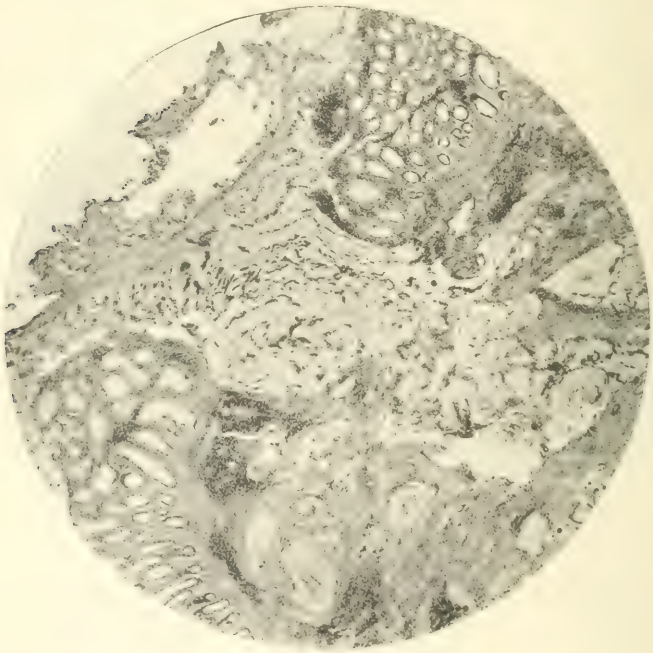
REMARKS ON THE ORIGIN OF "COLLOID CARCINOMA OF THE PERITONEUM."

JAMES EWING, M.D.

Since the widespread occurrence of endothelioma has become recognized, considerable question has arisen regarding the true nature of the well known forms of colloid cancer of the peritoneum. The older text-books uniformly state that these tumors are derived from the epithelial lining of the intestines, or from the ovary. Two or three years ago Dr. Jeffries presented to the Society a specimen consisting of an enormous number of small pearl-like masses scattered over the entire peritoneal surface. Although the growth had apparently

* The corrected dye ready for use has been placed upon the market.

originated in the stomach and had considerably infiltrated its wall, the wide diffusion of many such neoplasms over the peritoneum in other cases in which no intestinal tumor was dis-



EARLY CARCINOMA GELATINOSUM OF THE COLON.

covered was held to indicate that such tumors may sometimes originate in the peritoneal lining endothelium. This suspicion had been strengthened in the speaker's mind by having searched through the entire length of the gastro-intestinal tract in two cases in male subjects, without finding any initial lesion

in the mucosa. Moreover these tumors did not show the usual malignant tendencies of carcinoma reaching a very wide distribution before killing the patient, and showing no tendency to occlude the intestine or to invade its wall from without. Recently, however, he had encountered a small tumor of the *caput coli* plainly originating in the straight tubular glands of the colon but causing comparatively little destruction of the mucosa while making its way more especially through the muscular coat to the peritoneum. It showed throughout the structure of colloid carcinoma, while on the peritoneum there were a few of the typical pearl-like masses. As the tubular glands became involved in the tumor their cells increased in size, assumed a gelatinous character, and gradually became fused with the colloid mass (see microphotograph, by Dr. B. H. Buxton). This specimen served clearly to demonstrate that the colloid cancer of the peritoneum may originate in a small tumor-focus in the intestinal mucosa.

Two other specimens illustrating another type of cancer of the colon were presented. One of these exhibited the ordinary structure of malignant *adenoma destruens*, but of rather unusual papillary type. Moreover, at the base of the tumor the muscular coat was infiltrated with many small groups of cells rarely appearing in alveolar form. This tumor showed no trace of gelatinous degeneration which practically never occurs with *adenoma destruens* of the colon. A third specimen was presented showing a flat ulceration of the rectum 4 cm. in diameter, the structure of which was identical with that found in the growth infiltrating the muscularis of the second case. (*adenoma destruens*). This was the first indication which he had encountered that the *adenoma destruens* and the flat carcinomatous ulceration or "infiltration carcinoma," of the rectum were identical tumors.

From these three specimens the conclusion was drawn that three varieties of tumors arise from the cells of the straight tubular glands of the colon, viz.: (1) Gelatinous or colloid cancer, which early involves the peritoneum. (2) *Adenoma destruens*,

(3) Infiltrating carcinoma, which involves considerable areas of the muscular coat, splitting up its fibres, and frequently appearing as a flat carcinomatous ulcer in the rectum.

From the fact that gelatinous degeneration is very prominent in the first type, and is very rarely seen or occurs in a slight degree only in the two latter types, the conclusion was drawn that the gelatinous tumors arise from the mucus-secreting-cells of the intestinal glands, while the other forms develop from the ordinary lining cells of the glands which do not secrete mucus.

The first two cases were from the collection of Dr. B. H. Buxton, who also made the accompanying microphotograph.

Dr. Ewing presented gross and microscopical specimens illustrating the origin of colloid or gelatinous carcinoma of the peritoneum, and the relation between *adenoma destruens* and infiltrating carcinoma of the intestine.

ENDOTHELIOMA OF THE BREAST.

EUGENE HODENPYL, M.D.

The speaker, on presenting this specimen, said that it was his rule not to make a diagnosis of endothelioma if there was any good reason for calling a tumor anything else. The specimen presented was a tumor of the breast, and he thought it could hardly be called anything else but an endothelioma, although similar growths had been reported as "villous carcinomata." The specimen had been taken from an unmarried woman aged sixty years, who had noticed a lump in the left breast for four years before the operation. This had gradually enlarged until the entire organ became involved. There had been no emaciation or cachexia; and no involvement of the axillary lymph nodes was noted. The radical Halsted operation had been done. After the removal of the breast it was found that almost the entire breast was involved. The tumor was nodular in character, and in places there were hemorrhages and considerable gelatinous infiltration. On section the tumor resembled in its general appearance a papilloma;

but in the outlying portions one could see fairly large alveoli, usually lined with a single layer of cells. Some of these cells were almost cylindrical in character. In the smaller alveoli, in the periphery of the tumor, where the nature of the growth could be more conveniently studied, there was seen a distinct cell lining to the spaces; within the latter were often seen smaller spaces which were always found empty. Under the microscope the growth bore no resemblance to ordinary carcinoma, and the diagnosis of endothelioma seemed to be warranted.

Discussion.

Dr. EWING: I have had an opportunity of carefully studying this tumor of the breast, and it certainly looked very much like an endothelioma; yet I have seen in the past year or two several tumors which had approached this in type but were probably adeno-carcinomata. However, in neither of these cases had there been the same diffuse growth of cells.

A VERY LARGE CYST OF THE KIDNEY REMOVED BY OPERATION.

EUGENE HODENPYL, M.D.

This was a large multilocular cyst of the kidney which had been taken from a woman fifty-eight years of age, who for fourteen years had noticed a gradual enlargement of the abdomen, principally on the left side. The urine had been examined several times before the operation, and had been found about normal in quantity and in composition. The woman had done well for thirteen days after the operation. The urine had been examined daily, and for a few days contained a slight trace of albumin and a few red cells which had probably arisen from the effect of the operation and the ether. On the thirteenth day following operation she was suddenly seized with intense pain over the heart, and within five minutes died. No post-mortem examination was

permitted. The tumor retained the general shape of the kidney, and at one end a small portion of the parenchyma of the kidney could be discerned. When fresh the kidney weighed seven pounds and a half, and measured thirty inches in circumference, eleven inches in its longest diameter, and six inches in depth. It was almost impossible to say whether the cystic condition was acquired or congenital. The speaker was disposed to look upon it as an acquired condition, arising from obstruction produced by a calculus or other obstruction in the ureter.

RUPTURED ANEURISM OF THE BASILAR ARTERY.

O. H. SCHULTZE, M.D.

This was a specimen of fusiform aneurism of the basilar artery. It had been taken from a well-nourished man twenty-eight years of age, who had suddenly collapsed while engaged at his work as stoker on a tugboat. No further history had been obtained. The examination showed that the immediate cause of death had been asphyxia. The blood was fluid, and there was passive hyperæmia of all the organs. Evidence of syphilis was especially looked for, but not found. A small rupture was found with a subpial clot at the base of the brain, and this was the only blood found coagulated in the body. There was a rupture through the roof of the fourth ventricle into the ventricles, which were filled with blood. The aorta showed a marked hypoplasia, corresponding in development with that of a young adult woman. The valves of the heart were normal, and the heart itself weighed twelve ounces. The external genitalia were undeveloped.

SACCULATED ANEURISM OF THE MIDDLE CEREBRAL ARTERY.

O. H. SCHULTZE, M.D.

This sacculated aneurism of the right middle cerebral artery was located near the origin of the vessel. The ruptured portion

was covered by a blood clot under the pia, lacerating by compression the cortex of the inner aspect of the right temporal lobe and the pia mater. A very large clot had formed, covering the entire upper and outer surface of the right cerebral hemisphere. The aorta in this case also was markedly hypoplastic, corresponding in development to that of a young adult woman. The muscles and the valves of the heart were quite normal. The aorta showed a very minute lesion of atheroma on the inner aspect of the first portion. There was no history obtained in connection with this case. The man was apparently about thirty years of age, and his muscular development was good. The blood was fluid, and showed that death had occurred by asphyxia from compression of the brain. The specimens were interesting, as showing the absence of arteriosclerosis. These cases, the speaker thought, presented an argument in favor of under development of the arterial system, congenital if not hereditary in origin, as an etiological factor in the formation of aneurism.

A SPECIMEN OF A TUBERCULOUS APPENDIX.

L. T. LE WALD, M.D.

This specimen of a tuberculous appendix, was obtained from a case of pulmonary tuberculosis. Practically the only tuberculous process in the intestine had been in the appendix. The latter was about the size of the index finger, and contained several tuberculous ulcers. Several tubercles were found on the surface of the appendix. There was nothing in the clinical history which suggested tuberculous or other involvement of the organ.

TWO CONGENITAL CYSTS OF THE KIDNEY.

L. T. LE WALD, M.D.

Both specimens were taken from an adult about forty years of age. The kidney on each side was markedly cystic, in spite

of the fact that the person had lived to this age. The kidney tissue was found only in the strands between the cysts. Apparently they were of congenital origin. The nature of the urine excreted by this person was not known.

TWO CASES OF LARGE UTERINE FIBRO-MYOMATA COMPLICATED BY PREGNANCY.

L. T. LE WALD, M.D.

The first specimen was from a woman of thirty-eight years. Owing to the very rapid enlargement of the uterus an examination had been made by Dr. Studdiford, and it had been decided to terminate pregnancy. This had been done at the end of the third month. In the second specimen it seemed impossible that pregnancy could have gone on much farther after the time the laparotomy had been decided upon. The woman was thirty-five years of age, and had been operated upon by Dr. Coe

PRESENTATION OF SPECIMENS OF HYPERTROPHIED PROSTATE.

A. E. THAYER, M.D.

A number of bladders were exhibited to show prostatic disease and certain other interesting features. The first specimen showed ordinary hypertrophy of the middle lobe of the prostate, constituting the so-called "ball valve." In the second specimen hypertrophy of the lateral lobes was quite marked, while there was very little in the middle lobe. In another specimen the consistency of the tumor was such as to suggest sarcoma, but the microscope showed it to be an example of ordinary prostatic hypertrophy. Another specimen had been taken from a negro about sixty years of age. This man had been admitted to a hospital, complaining only of extreme

weakness. Physical examination of the lungs had shown apparent consolidation on the right side. The temperature had varied between 100° F. and normal. The urine examination had been negative. In two or three days there had been a sudden rise of temperature, shortly followed by death. At the autopsy the lungs had been found to be free from pathological change, except a small area of latent tubercle at the right apex. In the large intestine were old and deeply pigmented tuberculous ulcers, and a gangrenous colitis. In the bladder were 40 or 50 c.c. of pus; and on the posterior wall was a recent slough. In the trigone were a number of tubercles. The prostate was hypertrophied. Marked chronic nephritis was also present.

Proceedings

of the

New York Pathological Society.

New Series, Vol. I. March, 1901. No. 2.

TABLE OF CONTENTS.

Blumer, The Bacteriology of Lobular Pneumonia, Especially in Adults.—Thayer, A Case of Primary Carcinoma of the Liver.—Janeway, A Case of Lymphatic Leukæmia.—Schultze, Two Specimens of Aortic Aneurism.—Boldt, A Specimen of Urinary Organ Tuberculosis; Removal of Uterine Carcinoma by the Cautery; A Specimen of Gonorrhœal Salpingitis.

Dr. Edward K. Dunham, *President.*

THE BACTERIOLOGY OF LOBULAR PNEUMONIA, ESPECIALLY IN ADULTS.

GEORGE BLUMER, M.D.,

OF ALBANY, N. Y.

*Abstract.**

The bacteriology of the lobular form of pneumonia has been mainly worked up in its relation to the diseases of childhood, and especial attention has been given to lobular pneumonia following diphtheria and acute exanthemata. The question of the bacteriology of lobular pneumonia in adults has been the subject of relatively few researches. In looking over a series of three hundred and fifty records of autopsies performed in Albany, most of them in connection with institutions having

* Read by invitation before the Society, March 13, 1901. This paper will appear in full in the *Albany Medical Annals*, August, 1901.

an acute service, but some of them private autopsies, the frequency with which lobular pneumonia has been observed appears to be somewhat unusual. Among the three hundred and fifty autopsies lobular pneumonia was present in one hundred and fourteen, a percentage of just about 32.5. In the same group of autopsies there were but fifteen cases of acute lobar pneumonia, a percentage of 4.2. In seventy-two cases showing lobular pneumonia cultures had been made not only from the lungs but also from the organs in general. In the other cases cultures were not made, either because the bodies had been embalmed or because distinct evidences of post-mortem change were present.

The cultures were taken from the lung at the time of autopsy by burning the surface with a red-hot knife, a puncture being also made through the burned area with a red-hot knife. The culture was taken from this puncture. Cultures were made on agar or blood serum slants, preferably the latter, and the organisms isolated were studied on different media. The tubes made at autopsy were usually plated subsequently, and if any doubt as to the identity of an organism existed animal inoculations were resorted to. Cover-slips were made in some cases, but unfortunately not in all. The naked eye diagnosis of lobular pneumonia was in every instance confirmed by the microscope.

In our own series of seventy-one cases fifty-three were in adults. Thirty-three of these were single infections. The bacterial incidence was as follows:

Streptococcus	9
Colon	8
Staphylococcus aureus	7
Proteus vulgaris	3
Pyocyaneus and paracolon, each	2
Pneumococcus and staphylococcus albus, each	1

The bacterial incidence in the twenty cases of mixed infection was as follows:

Colon and aureus	4
Colon and streptococcus	3
Aureus and streptococcus	3
Colon and pneumococcus	2
Colon and citreus	2
Typhoid and streptococcus	2
Colon and pyocyaneus, each	1
Pneumococcus and pyocyaneus, each	1
Colon and albus, each	1
Lactis aerogenes and streptococcus, each	1

The literature dealing with lobular pneumonia in childhood relates chiefly to the forms following diphtheria and the exanthemas. Netter, Neumann, Quesner, and Durck, however, take up the subject from a general standpoint.

In comparing our results with those of others it may be seen that in our cases the pneumococcus is a rather rare organism, as is Friedländer's bacillus, while other organisms which are rarely met with in other reports are relatively common, such for example are the pyocyaneus and the proteus vulgaris. Further, the colon bacillus was observed quite frequently both alone and in combination in our series. Thus, in the adult cases the colon was present in eight out of thirty three single infections and in thirteen out of twenty mixed infections.

The rarity of the pneumococcus is explicable on several grounds. It occasionally fails to grow on media even at incubation temperature, and would thus be missed in cases without cover-slip control. It is easily outgrown by other organisms, especially the colon bacillus which was present in quite a large per cent. of our cases. The rarity of Friedländer's bacillus is not explicable in like manner. Perhaps the suggestion is not too far fetched, that there is to a certain extent a geographical distribution of bacteria, and that organisms which are common in one locality are rare in another. In a series of about two hundred and fifty autopsies studied bacteriologically we have observed Friedländer's bacillus but four times, whilst the bacillus pyocyaneus has been met with in over twenty five autopsies out of this number. The great infrequency of lobular

pneumonia in our autopsies would suggest that perhaps pneumococcus infections are more uncommon here than in New York, for example. Several practitioners in Albany have stated to me that many of the cases of lobular pneumonia seen there are atypical in their physical signs and do not show the characteristics of frank pneumonia. A comparison between New York and Albany as regards the death rate from acute respiratory diseases shows that in some months the death rate is three times higher per one thousand of population in New York than in Albany. Unfortunately these statistics do not separate lobar from lobular pneumonia.

The frequency of the colon bacillus is we think largely due to agonal or post-mortem invasion. This is shown in our series by a comparison of the lung bacteriology with the general bacteriology. Thus, in the fifty-three lobular pneumonias in adults the colon bacillus was present either alone or with other organisms in twenty-one. In twelve of these cases there was a general colon invasion. In seven out of the eight simple colon lung infections there was a general distribution of the colon bacillus throughout the organs. In the eighteen cases in children the colon bacillus was present in five and in two of these there was a general colon invasion. That the colon bacillus could have entered the lungs in the remaining cases by the upper air passages seems quite possible since Grimbert and Choquet claim that it is frequently present in the mouths of healthy people. Whether it is present as the cause of the lesion or merely as a secondary invader in lobular pneumonia is difficult to say. On the one hand there are undoubtedly colon bacilli of marked virulence, and on the other the colon is notorious as an organism which frequently overgrows other bacteria of common pathogenic import and masks infections by them. In lung infections the pneumococcus is so frequent and so easily masked by other invaders that it would seem almost certain that in some cases where the colon only was found it had displaced the pneumococcus.

In connection with the bacteriology of lobular pneumonia

the question of bacteria in normal lungs and in congested or œdematous lungs is of interest. The majority of the writers on the bacteriology of the normal lungs seem to incline to the belief that during life they are sterile. Ritchie in his recent careful study comes to this conclusion and several other authors agree with him. Beco after a careful study concludes that normal lungs can be sterile, but that they frequently contain bacteria of the varieties which are usually associated with broncho-pulmonary infections. Durck who studied the subject in connection with his work on broncho-pneumonia seems to think that the great majority of healthy lungs contain bacteria and largely pathogenic varieties. Both Beco and Dürck seem to regard the air passages as the source of these bacteria, and with normal lungs from healthy men or animals this doubtless is their most probable origin, colon invasions being excepted. In dealing with diseased individuals the question of the pulmonary infection being part of a general infection must be considered. With the object of determining the bacteriology of the lung in acute and chronic passive congestion, in œdema and in combinations of these conditions, I have examined a number of lungs in which these conditions were present.

Of twenty lungs which were acutely congested, six were sterile. The other eighteen contained bacteria of the following varieties:

Colon alone in six cases, with aureus in three, with albus in one, with Friedländer in one. Streptococcus alone was found twice, and aureus, B. typhoid, lactis aerogenes, and Friedländer each once. In all but six of these cases there was a general infection besides pulmonary infection. Of these six the infection was colon in one, lactis aerogenes in one, aureus in three, albus in one. In none of the six cases was there any evidence of bronchitis microscopically. In three out of the cases with general infection some of the alveoli contained besides blood a small number of polynuclear leucocytes. Perhaps this should be interpreted as indicating an early stage of pneumonia.

Of six cases of chronic passive congestion examined all were sterile, a somewhat suggestive fact taken in connection with the well-known relative resistance of such lungs to tuberculous infection.

Of four cases of œdema examined all contain bacteria. In one the pneumococcus was found, in two the proteus vulgaris, and in one the aureus and colon. The cases with aureus and colon showed a general colon invasion, and in one of the proteus cases there was a general proteus invasion. This left three out of the four cases with a local infection without general infection, and in none of these was there evidence of bronchitis.

Seventeen lungs which were both œdematous and congested were examined and only two were sterile. Colon alone was found in nine cases, but in seven of these there was general colon invasion. Colon was also found once with aureus and once with albus, but here again there was general colon invasion. The typhoid bacillus and the aureus were each found once associated with general infection with the same organisms. Of the fifteen cases in which bacteria were present only six were cases of pulmonary without general infection, two being associated with colon, three with streptococcus, and one with aureus. In one colon case a definite bronchitis was present, but in the other cases the bronchi was normal.

Four normal lungs were examined. All contained bacteria. One showed colon alone, two colon and albus, and one streptococcus. In all of the cases where colon was found there was a general invasion, and in one albus case there was a general albus infection. In two cases, one associated with albus and one with streptococcus, there was no general infection and no microscopic evidences of bronchitis.

These results show that both in normal and congested and œdematous lungs in patients dying of disease, the bacteria present in the lung are often present in the general system also, and are perhaps carried to the lung by the circulation. It is difficult to deny that the opposite may not sometimes be the case, the bacteria being carried from the lung into the general

circulation. In some of the cases described definite foci of infection were present in the body aside from the lung, but in others no such localized inflammatory condition was present, and it seems not unlikely that in some cases of general sepsis the lungs may be the point of entry of the infectious agent, and yet show no change beyond congestion or œdema.

In this connection the relation of the infection in lobular pneumonia to general infection is of interest. Aside from the colon cases, which have already been described, a good many of the cases of lobular pneumonia were associated with general infections. Pearce seems to be the only writer who discusses this association. He states that in his cases where a local or general infection existed, the broncho-pneumonia was due to the same organism, and this in general has been our experience. Our experience does not, however, coincide with his second statement that in chronic diseases, as Bright's disease and chronic heart disease, the broncho-pneumonia was due to the pneumococcus.

In our cases of simple lung infection, general infection was present in nine out of fourteen streptococcus cases, in four out of nine aureus cases, in all of three proteus cases, in one out of three pyocyaneus cases, and in single albus and pneumococcus cases.

In the mixed infections at times there is a generalization of both organisms, but at times only one of the two is generally distributed. Thus, in two colon and citreus infections the citreus was generally distributed in both, in five colon and streptococcus infections both organisms were generally distributed in two, whilst in a third the colon alone was generally distributed. In many of these cases the lung lesion was the only local evidence of infection, and doubtless the general distribution took place from it. It is questionable, however, whether the general distribution in some of these cases was not merely an agonal or post-mortem invasion rather than a true septicæmia.

The relation of the distribution and the histological character

of the lesions of lobular pneumonia to the type of infection has been noted both by Netter and Durck. Netter studied particularly the relation between the anatomical distribution and type of infection, but was able to make out no definite relation between different types of the disease and specific micro-organisms. Durck studied the relationship from the histological standpoint, and also concluded that very varied pictures could be produced by the same organism, and that there was no definite relation between specific bacteria and specific types of exudation. The study of our cases has led us to agree with both of these statements, and we would further support the statement of Durck that from a histological standpoint the exudate in lobular pneumonia cannot be differentiated from that of true lobar pneumonia in many instances.

The adult cases of lobular pneumonia were finally taken up from the standpoint of disease association, and particularly with regard to the bacterial associations occurring as terminal infections in typhoid fever and chronic diseases. Our object, particularly in the case of chronic diseases, was to determine the relation of the lung lesion to general infections, and to ascertain whether there was any particular bacterial association with specific diseases or disease group.

Eight cases of broncho-pneumonia complicating typhoid fever were studied. In these the typhoid bacillus was present twice, both times with the streptococcus. The colon bacillus was present four times, twice alone, once with the aureus and once with the pneumococcus. The pyocyaneus was present in one case and one case was sterile. In one of our cases in which the typhoid bacillus was present there was typhoid septicæmia, in the other a general streptococcus septicæmia.

Besides typhoid fever the relation of broncho-pneumonia to chronic diseases of certain types was studied.

In ten cases of chronic nephritis with broncho pneumonia the colon bacillus was found in six, alone once, twice with the citreus, and three times with the aureus, albus, and pyo-

cyaneus respectively. The aureus was found alone once, once with the streptococcus, and once with the colon. The streptococcus was found once alone and once with the aureus. There was a general infection in seven of these cases, twice with the staphylococcus citreus, twice with the staphylococcus aureus, and once each with the streptococcus, colon, and pyocyaneus respectively.

In six cases of lobular pneumonia with arterio-sclerosis the colon bacillus was found four times, twice alone, and once with the pneumococcus and aureus respectively. Of the other two cases one showed streptococcus, the other proteus. There was general infection in three of these cases with the pneumococcus once, the proteus once, and the colon and aureus once.

Six cases of lobular pneumonia complicating cerebral lesions showed the aureus four times, and the colon and the streptococcus once each. One aureus and one colon case showed general infection.

Three cases of lobular pneumonia in cirrhosis of the liver each showed the colon bacillus, alone twice and once with streptococcus The last-named case only showed general infection, and that with colon.

These results show that in terminal broncho-pneumonias in chronic disease the pulmonary infection was associated with a general infection in sixteen out of twenty-five cases. They also showed that there is no particular bacterial association with specific diseases or diseased groups. The apparent exception was the broncho-pneumonia associated with cerebral lesions in which the staphylococcus aureus was found in four out of six cases. This number of cases is too small a one from which to formulate conclusions, and this finding is not corroborated by the cases of Pearce and Kreibich. The main conclusion to be drawn from these cases would seem to bear upon the relation between congestion and œdema of the lungs, and lobular pneumonia on the one hand and general infections on the other. The cases seem to show that with merely congested or œdematous lungs, as with broncho-pneumonia, a general infection is

frequently present. As in many of these cases no bacterial lesion can be found aside from the pulmonary one, it seems likely that the lungs are much more frequently the portal of entry in general infection than is generally supposed, and that often without marked pulmonary lesions.

Discussion.

Dr. A. J. LARTIGAU: By this communication Dr. Blumer has added another important contribution to our knowledge of the bacteriology of lobular pneumonia. I have been particularly interested in a geographical distribution of pathogenic micro-organisms, to which allusion has just been made. My own experience with reference to the variations in the numerical frequency with which the different members of the pyogenic group of organisms is encountered in different localities agrees fully with that of Dr. Blumer. In comparing previous experience in Albany with that in New York City, the relative infrequency of the bacillus pyocyaneus in the latter place, for instance, is very striking. On the other hand, it seems to me that the diplococcus lanceolatus is met with more constantly in New York in ordinary post-mortem bacteriological work than in Albany, where the streptococcus is by far the predominant organism in cases of pneumonia. Such apparent differences of bacterial distribution may in some measure account for the high streptococcus figures in the series of cases presented this evening by Dr. Blumer. But even taking this into consideration, it seems to me that the pneumococcus would have been found with much greater frequency if more elaborate methods of investigation had been practicable. Similar work in other classes of lesions has recently shown that by the use of a greater variety of media and more comprehensive and elaborate methods of technique the pneumococcus is present much more frequently than hitherto suspected.

With reference to the presence of micro-organisms in the

normal lung. I may say that investigations recently made by myself confirm, on the whole, the observations of Beco, who found that normal lungs are ordinarily germ free, although occasionally pneumococci and colon bacilli may be present.

Dr. Martha Wollstein: I have been especially interested in the bacteriology of pneumonia in infants. At one time I had examined bacteriologically one hundred broncho-pneumonias of infants. They had been divided into primary and secondary cases. The primary had shown the pneumococcus present in more than seventy-five per cent.; the secondary cases in a very much smaller percentage. The pyocyaneus had been found three times in the secondary cases. It had been found better to avoid the use of hot knives (or to burn the surface of the organs), but to sterilize the knives in metal boxes, and to use them at the autopsy perfectly cool. It was extremely rare to find a perfectly healthy lung in an infant at autopsy, but in a few instances such lungs had been met with, and had been found sterile.

Dr. Charles Norris: I have often found it very difficult to differentiate between streptococci and pneumococci, and this has led to much confusion.

Dr. James Ewing: I should like to draw attention to the use of the terms lobular and broncho-pneumonia as synonymous, a usage which has led to some confusion owing to the fact that some pathologists believed that a distinction should be made between them. My impression is that Dr. Blumer included both simple exudative lobular pneumonias and the other type of circumscribed pneumonias. I have been struck with the conclusion of the author that the lungs often served as portals of entry for germs in terminal septicæmias.

Dr. George Blumer: Many writers on this subject have made use of only one culture medium. I have been interested in the point made by Dr. Wollstein regarding the possible destruction of some of the pneumococci by the use of hot knives. My paper included both lobular and broncho-pneumonia, though I believe with Dr. Ewing that there is a

distinction between these two forms. I have used these terms interchangeably because most of the cases hitherto reported had included both varieties.

A CASE OF PRIMARY CARCINOMA OF THE LIVER.

A. E. THAYER, M.D.

The specimen of carcinoma of the liver presented was taken from a woman about forty-five years of age. She had entered a hospital about two weeks before death, complaining of some abdominal distress, and examination had shown marked ascites. She had been tapped, and about fourteen quarts of blood-stained serum removed. Through the puncture there had been discharged considerable fluid — a quantity estimated to be as much as that removed by tapping — but this latter fluid had not been blood-stained. The woman was obese and not particularly anæmic. There was slight jaundice of the conjunctiva and in patches over the abdomen. On autopsy, about 1500 c.c. of clear serum were found in the peritoneal cavity. There was a broad band of small varicose veins along the reflection of the visceral peritoneum to the parietal layer. The liver was not especially enlarged. In the right lobe was a well-marked cirrhosis; and comparatively little tumor involvement of this portion was noted. The left lobe was for the most part replaced by nodules of neoplasm. The round ligament was enormously increased by fat and connective tissue, and on each side were prominent varicosities. With the exception of its shrunken condition the stomach was normal. There was no neoplasm in the duodenum. Microscopical sections of the pancreas had shown no distinct evidence of carcinoma. A careful search showed that the stomach, liver, pancreas, intestine, and the adrenals were not affected by the neoplasm, from which it was assumed that the tumor was primary in the liver. The larger masses were of a mottled red color, and on being scraped yielded very little fluid. On section

through the liver, a large mass was found near the hilus. It was yellow in color, and contained a thrombosed portal vein. Another such mass was found in the hepatic vein. The speaker thought there had been first a cirrhosis of the haematogenous variety, and that from the newly proliferated bile ducts the neoplasm had originated which had through the portal vein given rise to the very rapid metastasis. Sections were exhibited under the microscope.

Discussion.

Dr. O. H. SCHULTZE: The invasion of the portal vein was a very interesting feature, and probably explained the rapid extension of the growth, particularly into the left lobe. The question might arise as to whether the growth had started directly in the hilus or had originated in the pancreas or somewhere else in the vicinity. There might certainly be a transition between the ordinary proliferation of the bile ducts in cirrhosis of the liver and primary adenocarcinoma.

Dr. JAMES EWING: Well-authenticated cases of primary carcinoma of the liver are so few that it seems wise to take extraordinary precautions to make sure of this diagnosis before it is placed on record. This specimen shows a totally different arrangement from the usual form of hepatic carcinoma. It might belong to the cells of the gall duct or the pancreas, probably the latter. After a close study of the tumor I do not feel that the question has been fully decided. A very exhaustive examination of the pancreas would be required.

A CASE OF LYMPHATIC LEUKÆMIA.

T. JANEWAY, M.D.

This case was interesting in showing that a sharp line could not be drawn between acute and chronic lymphatic leukæmia. The subject of this report was a boy of six years. The trouble had begun three months previously with a swelling over the

masseter muscle, and one month later the glands of the neck had become enlarged. The boy had then developed a marked pallor. Other glands became palpable, but no mediastinal glands were thought to be enlarged. There had been no hemorrhages, and there was no leukæmic retinitis. The blood examination showed 40 per cent. of hæmoglobin with a normal number of cells. There were 219,000 white cells, of which 98 per cent. were lymphocytes, and of the latter nearly 87 per cent. were of the large variety. The red cells were moderately pale. The result of this examination pointed to a typical acute leukæmia, yet the boy presented clinically a moderately progressive leukæmia. Cases of this kind compared with cases of chronic leukæmia of long duration seem to show that it was impossible to classify acute lymphatic leukæmia as a separate disease. Specimens were presented under the microscope.

Discussion.

Dr. JAMES EWING: Fraenkel's own countrymen have not accepted his claims regarding the significance of large lymphocytes in leukæmia. Fraenkel has stated that acute leukæmia is always lymphatic, and when acute is always characterized by the presence of large lymphocytes. Rosenfeld has recently claimed that when lymphatic leukæmia affected the lymph nodes and the spleen, and other lymphatic structures excepting the marrow, it is chronic in course and marked by the presence of an excess of small lymphocytes; and that when it affected the marrow exclusively or chiefly that its course is acute, and marked by severe anæmia and an excess of large lymphocytes.

Dr. T. JANEWAY: I saw a few years ago a case of lymphatic leukæmia which had run eighteen months with enormous enlargement of the superficial glands, and yet the blood examination had shown a good proportion of large lymphocytes. I have seen eight cases of lymphatic leukæmia in the last few years, and they have presented every possible variety of blood picture.

TWO SPECIMENS OF AORTIC ANEURISM.

O. H. SCHULTZE, M.D.

The first was a fusiform aneurism of the first portion of the arch of the aorta, with rupture of the right side adjacent to the right auricle and the superior vena cava. The specimen had been taken from a woman fifty years of age. There was an enormous hæmopericardium with resulting compression of the heart, thus inducing death. The second specimen was a sacculated aneurism proceeding from the posterior aspect of the first portion of the arch of the aorta, and showing a marked transverse opening. It was possible that trauma might have been the cause of the rupture. In both cases there had been no positive evidence of syphilis. The first case showed marked arteriosclerosis of the abdominal aorta and a beginning aneurism at the cœliac axis. There was also chronic interstitial nephritis. In the second case there had been only a general passive hyperæmia of all the organs. This patient was a man aged thirty-five years. The aneurism had ruptured adjacent to the right auricle and superior vena cava. In this case also the immediate cause of death had been the pressure exerted by the blood which had accumulated in the pericardium. In both cases death had occurred suddenly and no clinical history had been obtainable. The speaker thought that the old notion about arteriosclerosis being the greatest cause of aneurism had been exploded.

Discussion.

Dr. L. Le Wald: I recall a case of aortic aneurism that had ruptured while the patient was engaged in the act of defecation. The rupture had occurred in the last portion of the thoracic aorta and in close relation to the diaphragm. In that case there had been a distinct arteriosclerosis and a history of syphilis.

Dr. H. Brooks: I presented three years ago three speci-

mens of small sacculated aneurism of the ascending arch very similar to the second case presented by Dr. Schultze. In these I had studied carefully the histology of the aneurismal sac and of the walls of the aorta. The arteriosclerosis of the larger arteries in these cases had not been extensive, but of a patchy character; and the bases of the aneurisms had been chiefly involved. In those cases the arteriosclerosis had apparently been the cause of the aneurism. All of the subjects in this series were young persons.

Dr. SCHULTZE: The statement that one of the aneurisms was probably of traumatic origin had been based on the fact that the longer diameter of the opening, which was oval, was almost strictly in the transverse axis of the aorta. By the term "trauma" it was not meant that any direct force had been exerted from without, but rather that work involving considerable physical exertion might have subjected the arch of the aorta to severe pressure. If a tear occurred under these circumstances it was more likely to be in the transverse diameter. Although much arteriosclerosis was frequently seen with aneurisms, it was also true that a very excessive degree of arteriosclerosis was often observed without the occurrence of aneurism. Dr. I. Adler had recently raised the question as to the rôle played by the yellow elastic fibre in the aorta in connection with the formation of aneurisms. It was known that vesicular emphysema was hereditary, apparently as a result of the quality or congenital weakness of the yellow elastic fibre, and it seemed not improbable that a similar relation might exist between this fibre and the development of the aneurisms.

A SPECIMEN OF URINARY ORGAN TUBERCULOSIS; REMOVAL OF UTERINE CARCINOMA BY THE CAUTERY; A SPECIMEN OF GONORRHŒAL SALPINGITIS.

H. J. BOLDT, M.D.

The first specimen showed tuberculosis of the kidney, ureter, and bladder. The tuberculosis had been diagnosed prior to death

during the examination for the pelvic ailment of which the patient complained. Suspicion had been aroused by the vesical symptoms and the thickening of the right ureter detected by bimanual palpation. It had been thought best first to operate for the pelvic disease, a suppurating ovary, and later to attack the renal and ureteral disease. Unfortunately the slipping of the ligature a few hours after the operation caused a fatal intraperitoneal hemorrhage. The interesting feature was the possibility in some instances of attention being directed to serious ureteral disease by a bimanual examination.

The second specimen illustrated the advantages of removal of the carcinomatous uterus with the aid of the galvano-cautery. The disease had begun in the cervix and unfortunately had advanced to such an extent that the result of radical operation seemed hopeless. From the observation of other patients operated upon by the speaker with the galvano-cautery, and the results achieved by Byrne, of Brooklyn, Mackenrodt, of Berlin, and others, he had been induced to attempt it in the present case. The advantage of extirpation with the heated knife was that the destruction of epithelial elements extended some distance beyond the line of cutting, but there was a disadvantage from the same source, *i.e.*, secondary breaking down from a burn or slough of other structures. This had happened to him in one instance. In that case the ureters had given way several days after the operation, yet in spite of this accident the patient had remained free from recurrence for four years, and was still well and enjoying good health. The ureteral lesions had been subsequently attended to by a colleague. The time consumed and the tediousness of this method of operation should not cause any hesitation in its adoption if it should be shown that the ultimate result was greater freedom from recurrence.

The specimen of gonorrhœal salpingitis was removed from a woman, thirty years old, who had been infected with gonorrhœa soon after marriage. The speaker had attended her in five attacks of intense pelvic peritonitis, and she had had several

others. She had been practically well since the performance of the radical operation for the removal of the uterus and appendages last November. At the operation it had been necessary, because of the extensive adhesions involving the adnexa, to bisect the uterus before its removal. The specimens presented showed the characteristic lesions.

Proceedings

of the

New York Pathological Society.

New Series, Vol. I. April, 1901. No. 3.

TABLE OF CONTENTS.

Minot, The Embryological Basis of Pathology.—Cordes, Congenital Occlusion of the Duodenum.—Schultze, Thrombosis of the Inferior Vena Cava.—Larkin, A Study of Two Cases of Hypertrophic Stenosis of the Pylorus.—Wood, A Note upon the Prognostic Value of the Diazo-Reaction in Phthisis; Primary Endothelioma of the Peritoneum; Pneumococcus Tricuspid Endocarditis.

Dr. Edward K. Dunham, *President.*

THE EMBRYOLOGICAL BASIS OF PATHOLOGY.*

CHARLES SEDGWICK MINOT, LL.D.

Embryology is the basis upon which pathological science must be erected. Pathology is even more a superstructure upon embryology than is anatomy. Anatomy, in its descriptive form, may stand by itself and have usefulness. Pathology cannot be built up as a merely descriptive science. It fails of its true purpose unless it discovers the causes of diseases. Now since function is dependent on structure, the aim of the pathologist must be, first, to discover the causes of morbid structure. In brief, pathology at the present time deals chiefly with problems of the development of anatomical forms. Pathology and embryology might almost be united in a single comprehensive study—morphogeny. Let us then try, for this

* The Middleton Goldsmith Lecture delivered before the New York Pathological Society, March 26, 1901.

evening at least, to free ourselves from the conception of an essential difference between normal and abnormal structure—a conception which, I believe, domineers too largely over our daily thoughts. This belief of mine I hope to justify to-night.

Simple description is indispensable, it furnishes the virgin facts; but facts do not develop by pathogenesis into science; they must be saturated with the stimulus of study, with the stimulus of knowledge of their history, their antecedents, their causation; then we may see them evolving themselves into new orders, which we call natural laws. As little as a description of the people of the United States with no information as to their history could satisfy a serious thinker, so little can descriptions of fully developed structures satisfy an earnest pathologist. An innate, intense mental impulse is continually driving us forward in the search for causes, and obedience to this impulse is one of the main factors in scientific progress. All this is familiar, trite even, but may serve to fix our starting thought, namely, that we are to study causes.

Our attention is to be directed to the consideration of what embryology can teach us in regard to the causation of organization, and then to the application of those teachings to pathology. This plan will exclude from our discussion many of the aspects of embryology which appeal most strongly to pathologists. We must omit from our study at least three groups of interesting phenomena, to wit: (1) The arrests of development; (2) the teratological formations, monstrosities, and misdevelopments, which will, however, have to be included ultimately even in the precise field we are about to study; (3) the so-called teratoma, or, to use a more recent term, "embryoma." I may say in passing that I find it very difficult to accept the hypothesis that these remarkable structures arise by a parthenogenetic development of ova, retained in the parent body. Professor Bonnet's hypothesis is more legitimate, but towards that also my attitude is one of sceptical agnosis. Bonnet suggests that one of the early segmentation cells (blastomeres) may become isolated and retarded in its

development, remaining as an inclusion in the fetal tissues, and afterwards develop and produce a variety of tissues, as isolated blastomeres have been shown by experiments on the lower animals to be capable of doing.

Teratological formations fall, it seems to me, naturally into three fairly definite divisions: (1) Those due to necrosis of the tissues, which apparently rarely if ever takes place uniformly throughout the embryo; (2) those due to gross mechanical disturbances of the development, consequent upon failure of the proper correlation of the growth of parts (monstrosities of this division are probably the most common); (3) errors in the differentiation of the tissue, or pathological histogenesis. It is only phenomena of the first and second divisions of teratology which we can safely drop from view, while those of the third division—errors in differentiation—we must bear uninterruptedly in mind.

One more preliminary explanation is necessary. The range of pathological changes is not so great as to reach equality with embryological developments. In the normal embryo we deal with the evolution of complete organs, together with all their accompanying varied and complex modifications of tissue. In pathology, on the contrary, we deal not with organs, but with modifications of tissues, with histogenesis. The statement will not seem too absolute if it is recalled that we have excluded arrests of development and monstrosities from our discussion.

Histogenesis is the common territory in which the pathologist and embryologist have—to borrow a legal phrase—an undivided interest. It is unfortunate that our tendency has so long been to attempt an unnatural and impossible partition of the territory, which has resulted only in a division of our forces into two camps, between which has reigned little interest and less sympathy. I venture to regard your invitation to address you to-night as a wish, which I fully share, to secure fuller co-operation between the two camps of workers, who are both striving to lay bare the laws which govern the differentiation of cells.

After these preliminary explanations it is possible to define the evening's task with precision. It is twofold: (1) To present some of the more important conceptions derived from embryological study in regard to the processes of cell differentiation; (2) to suggest some of the bearings of these conceptions on the problems of pathology.

Part I.—Normal Differentiation.

Under this head I propose to discuss three fundamental ideas: (1) Of the undifferentiated cell; (2) of the progress of differentiation; (3) of the changes which may succeed differentiation.

The fertilized ovum is an undifferentiated being, although it has a very complex organization, and contains, besides the protoplasm, a store of nutritive material, the so-called yolk or deutoplasm. As there is only one nucleus, there can be no variety of nuclei; the term "undifferentiated," therefore, applies to the protoplasm, which seems to have a uniform essential structure throughout, although the masses and strands of protoplasm may exhibit characteristic peculiarities, especially in relation to the distribution of the yolk. In the adult, on the contrary, the protoplasm of the cells of different tissues offers many varieties of essential structure, which can often be readily distinguished under the microscope. It is a legitimate conclusion that the absence of visible peculiarities of the intimate structure of the egg protoplasm, by which one part may be distinguished from another, corresponds to uniformity of structure throughout the egg — excepting, of course, certain special characteristic arrangements, as, for example, the centering about the centrosome, which may occur in any cell.

We have also direct experimental proof that the egg is uniform throughout, or, to use a better phrase, that the egg is isotropic. Pflüger, in 1884, proved that the side of the frog's egg which normally develops into the ventral surface of the embryo

can be made to develop into a perfectly typical dorsal surface. The frog's egg has a small white area, which normally lies underneath, the larger, darkly pigmented area of the egg alone showing from above. Out of the dark area the back, with the nervous system and other parts, takes its origin. If the eggs, freshly fertilized, are fastened with the white side up, then the white side produces an absolutely normal back and nervous system, normal as to form and function, though lacking the typical pigmentation. These observations were confirmed by Born, who further discovered that the segmentation nucleus always rises towards the upper side of the egg, and that the position of the nucleus determines which part of the ovum shall become the dorsal side of the embryo. Another set of experiments by Oskar Schultze demonstrated that both the unpigmented and the pigmented sides of the same egg could be made to produce dorsal structures.

Another class of experiments, which were first made by Hans Driesch, have demonstrated that the earliest cells (segmentation spheres, blastomeres, or cleavage cells, as they are variously called) produced by the ovum preserve the undifferentiated qualities of the parent egg, and may develop in one way or another according to circumstances. The egg of a sea urchin divides into two cells, each of which multiplies and normally gives rise to half * of the body of the animal. By somewhat violent shaking the two cells may be artificially separated; each cell may then develop into a complete larval sea urchin, but of half the normal size only. Similar experiments have since been made by several investigators, who have obtained like results with other animals, vertebrate as well as invertebrate. Even more remarkable larvæ have been raised from blastomeres of the four-cell and eight-cell stages of segmentation, producing larvæ of one fourth and one eighth the normal size. Zoja claims to have repeated the experiment successfully on the eggs of Clytia and to have obtained one sixteenth larvæ.

The facts offered suffice to illustrate the two aspects of our

* It would be safer to say supposedly about half.

conception of the undifferentiated condition of living matter. The first aspect is morphological and presents to us the apparent uniformity of the visible minute structure of protoplasm. While we readily admit that the uniformity may be only apparent in the sense that we fail to observe fine differences, yet we none the less maintain that the uniformity is real, because there is an absence of variations of structure comparable to the variations which we can observe in the cells of adult tissues. The second aspect is physiological and offers to our view the wide range of possibilities in the future developmental history and growth of the protoplasm. The fate of the protoplasm of any given part of the ovum is not fixed, but if its conditions of development are changed its fate is changed. A few years ago the mosaic hypothesis was advanced by W. Roux, and it has been vigorously defended by him. According to the mosaic theory, the egg is a mosaic pattern, each member of which has its predestined history. It is fortunate for our comprehension of pathological processes that we are already able to say that Roux's hypothesis is erroneous.

We must start then with the right conception of the ovum, every part of the protoplasm of which is to be regarded as potentially capable of producing any or all of the tissues of the adult.

We turn next to the consideration of the progress of differentiation, in order to establish a second fundamental idea, namely, that it acts as a progressive restriction of the further development. Each successive stage of differentiation puts a narrower limitation upon the possibilities of further advance. Applied to pathology this law means that the range of possible pathological changes is determined not merely by the nature or kind, but also by the stage or degree of the previous differentiation of the tissue.

The eggs of all animals* pass through two well-marked phases of development. During the earlier and much shorter phase, the nuclei are multiplying rapidly, while the cytoplasm is grow-

* The protozoa are obviously excluded from the present discussion.

ing but little, if at all. This period includes the time of segmentation, as commonly described, and somewhat longer. During this period the total bulk of the nuclei in proportion to the protoplasm is fundamentally changed. The ovum arises from a cell, the ovocyte, which, as its last act, grows rapidly; this enlarged cell by the process of maturation gives rise to the female sexual element, which has a single nucleus. After fertilization we have an ovum with much protoplasm and deutoplasm, but again with only the single segmentation nucleus. The development of each individual begins, therefore, with a cell in which the extreme disproportion between the size of the nucleus and of the whole cell body occurs. The first effort of development is to correct this disproportion by the enormously rapid increase of the nuclei, which continues until cells of the embryonic type are produced, that is to say, cells each with a minimal amount of protoplasm around the nucleus. With the production of cells of the embryonic type, the first phase of development is completed. The limits of this phase are very indefinite, for we observe often that the production of cells of the type defined may be far advanced in one part of the germ, while it is still in early progress in another. In fact the phase has no exact boundary in time.

During the second, later, and much longer period, or phase of development, the multiplication of nuclei lags behind the growth of the protoplasm, the increase is gradual and often shows itself through successive generations of cells, sometimes, however, in a single cell, which no longer multiplies. Of the first method of protoplasmic growth, embryonic blood cells offer a good illustration; of the second, the neuroblasts or young nerve cells afford a striking example. Now cells of the embryonic type show little if any capacity for differentiation, and the increase of the protoplasm in the single cell is, so far as we can judge, a necessary preliminary step to cell differentiation. The embryonic cells have yet another characteristic of basal significance they are capable of rapid multiplication. Hence we conclude that the growth of the cytoplasm impedes

the multiplication of cells, and therefore ultimately retards the growth of the body as a whole, while, on the other hand, it favors differentiation. Accordingly the growth of cells and their differentiation are essentially antagonistic processes, which are necessarily more or less mutually exclusive. This conclusion, which I published in 1890, has since been amply confirmed by further observation. It is probably applicable alike to animals and plants, alike to normal and to abnormal tissues. It is one of the many conclusions of embryology which are sure to throw a revealing light upon some of the dark problems of pathology.

During the first phase of development, as just defined, we encounter preparatory changes which we may characterize summarily as the manufacture of embryonic cells. During the second phase, though the production of embryonic cells is doubtless continued in certain regions, there supervenes the process of differentiation—the true histogenesis.

After segmentation there follows the formation of the germ layers, a gradual arrangement of the cells in three distinct primary strata; at least in all vertebrates there are always three strata, never more* nor less. The outer and inner layers, ectoderm and entoderm, very early become distinctly epithelial. The middle layers become partly epithelial, partly of a special character, that is, mesenchymal. At first one is inclined to think of the difference between epithelium and mesenchyma as a fundamental one, an early and unalterable separation of cells into classes. This view finds support in the fact that the mesenchyma, and it only, produces in the course of further development the connective tissue and supporting tissues of the adult. More attentive study of the germ layers in early stages reveals, however, that the mesenchymal cells arise from the epithelium; single epithelial cells migrating from the parent territory, while, on the other hand, groups of

* Hertwig and some other German embryologists divide the mesoderm into two layers; the division is contrary to the actual development, and is made, in my opinion, quite arbitrarily to satisfy the needs of an erroneous theory.

mesenchymal cells rearrange themselves so as to form an epithelial covering of some surface, as, for example, in synovial cavities, arachnoid spaces, the inner surface of the cornea, lymph vessels, etc. Such observations teach us that we must not assume that either one form or the arrangement of cells are necessarily and always a sign of true differentiation, but that instead we are to conceive of differentiation as a change in the intimate and essential structure of the individual cell, more specifically of its protoplasm, and perhaps of its nucleus. The rôle of nuclei in histogenesis is a topic which, unfortunately, is still awaiting serious investigation. To resume: It seems to me probable that the cells of the germ layers are at first quite indifferent, so that if it were possible to graft a young mesodermal cell on to the ectoderm or entoderm, it would become a true ectodermal or entodermal cell, as the case might be.

But although we may, so far as we now see, regard the cells in the germ layers as originally wholly indifferent as individual cells, nevertheless we must not forget that as members of a germ layer their potential fate is already restricted by the conditions of their very layership — if I may coin a word for the occasion. Each layer produces its own group of tissues, and never any other. There are indeed apparent exceptions to the rule, as, for example, the stratified, horny epithelium of the esophagus, which is strikingly similar to the epidermis, although in one case the tissue is ectodermal, in the other entodermal. We have, however, to do only with a resemblance, and the development in the two cases is quite unlike — the esophageal epithelium in the mammalian embryo being ciliated at one stage, and exhibiting then little resemblance to any stage of the epidermis.

Each germ layer has its specific function, its exclusive share in the work of differentiation. The work of one layer is not done by another nor shared by another. It is true that attempts are made from time to time to upset the validity of this fundamental doctrine, but they have hitherto failed to find support or recognition from any leading embryologist, and I deem

these attempts unworthy of serious consideration. We are able now to assign almost every cell of the normal adult human body to its proper germ layer. Our only great uncertainty is where two layers meet, as do the ectoderm and entoderm in the pharynx, or as do the mesoderm and entoderm where the ureter opens into the bladder. With these and perhaps a very few other small exceptions, everything in adult anatomy can be correctly stated in terms of germ layers. The layership of every organ is known, save that in the cases of the thymus gland, the tonsils, and the adrenals authorities are not yet agreed.

A remarkable attempt to upset the doctrine of the germ layers deserves brief consideration. It was first maintained by Goronowitch that the cells forming at least a part of the skeleton arose from the ectoderm. The same opinion was expressed also on the basis of their own investigations by H. Klaatsch and by Miss Platt. Confirmation of these views has not followed, but, on the contrary, C. Rabl, one of the most trustworthy of living observers, maintains that essential parts of Goronowitch's and Klaatsch's evidence are simply errors of observation. Klaatsch's views were based partly on the study of the developing teleost fins. R. G. Harrison has shown that here the German worker is in error. Miss Platt's observations were made in the head region of embryo Necturus. An examination of a number of series and stages has not enabled me to find the slightest evidence in favor of Miss Platt's conclusions. H. K. Corning has pointed out that the processes alleged by Miss Platt to occur in Necturus do not take place in the frog, *Rana temporaria*. We may, therefore, I think, safely regard this attempt to overthrow the morphological value of the germ layers as unsuccessful. I know of no other attempt of sufficient importance to be even mentioned.

The importance to pathologists of a thorough knowledge of the genesis of the tissues from their germ layers can hardly be emphasized too strongly, for it is more than probable that all pathological tissues are as strictly governed by the law of the

specific value of germ layers as are the normal tissues. Are there not many pathologists whose knowledge of embryology is wholly insufficient to meet the practical needs of their professional study even in this one direction?

The accompanying table presents the principal tissues, classified according to their layership. There have been classifications of organs on the layership basis published before, but inasmuch as organs usually contain cells from two layers, we get a more correct presentation of the actual genetic relationships by restricting our tabulation to the tissues. Leucocytes do not appear in the table for the reason that their first origin is uncertain. Blood cells arise very early, before the clear separation of mesoderm and entoderm has occurred; it is possible that they are entodermal. With these two limitations, the table presents our present knowledge.

CLASSIFICATION OF THE TISSUES.

A. Ectodermal.

(1) *Epidermis:*
- (*a*) Epidermal appendages.
- (*b*) Lens of eye.

(2) *Epithelium of*
- (*a*) Cornea.
- (*b*) Olfactory chamber.
- (*c*) Auditory organ.
- (*d*) Mouth (oral glands, enamel organ, hypophysis).
- (*e*) Anus.
- (*f*) Chorion, fetal placenta.
- (*g*) Amnion.

(3) *Nervous System:*
- (*a*) Brain: optic nerve, retina.
- (*b*) Spinal cord.
- (*c*) Ganglia.
- (*d*) Neuraxons.

B. Mesodermal.

(1) *Mesothelium:*
- (*a*) Epithelium of peritoneum, pericardium, pleura, urogenital organs.
- (*b*) Striated muscles.

(2) *Mesenchyma:*
- (*a*) Connective tissue, smooth muscle, pseudo-endothelium, fat cells, pigment cells.
- (*b*) Blood.
- (*c*) Blood vessels.
- (*d*) Lymphatics.
- (*e*) Spleen.
- (*f*) Supporting tissues, cartilage, bone.
- (*g*) Marrow.

C. Entodermal.
- (1) *Notochord.*
- (2) *Epithelium of*
  - (*a*) Digestive tract, esophagus, stomach, liver, pancreas, small intestine, yolk sack, large intestine, cecum, vermix, rectum, allantois (bladder).
  - (*b*) Pharynx, Eustachian tube, tonsils, thymus, parathyroids, thyroid.
  - (*c*) Respiratory tract, larynx, trachea, lungs.

We will now turn to the analysis of the differential process in each germ layer. We have to deal with changes in cells.

There are two distinct types of cell differentiation, which I think have not hitherto been clearly recognized or defined. For both types the starting-point is the same—the undifferentiated embryonic cell. In one type we find that as the cells proliferate a portion of them only undergoes differentiation, and another portion remains more or less undifferentiated, and retains more or less fully the power of continued proliferation. The epidermis is a good representative of this type. Its basal layer consists of embryonic cells, which multiply; some of these cells move into the upper layers, enlarge and differentiate themselves into horny cells; others remain in the basal layer and continue to multiply. The progeny of a given basal epidermal cell do not all have the same fate, but divide themselves into two kinds of cells, one kind retaining the ancestral character, the other becoming something new and unlike the parent cell. Differentiation according to the second type is characterized by its inclusion of all the cells. This type has its culminating and most perfect illustration in the central nervous system, where, comparatively early in embryonic life,

all the cells become specialized, and with acquisition of specialization they forfeit their power of multiplication—the neuroglia cells partly, the nerve cells wholly. The growth of the brain after early stages depends not on the proliferation of cells, but chiefly upon the increase in size of the individual cell. The correctness of this statement is not affected, in my belief, by the fact that epithelial portions of the medullary tube in comparatively late stages may be added to the nervous portion, the cells multiplying rapidly, as we see at the growing edge of the young cerebellum. The brain here grows by the addition of cells in the indifferent stage, but as soon as these cells are differentiated, they conform to the general law and divide no more (neurones), or slowly (glia cells).

The two types of differentiation produce essentially unlike conditions. The pathologist may not overlook such unlikeness with impunity. The two types pass into one another with many intergrades. Hence when we consider the possibilities of pathological alteration we must in each case seek to determine how far the condition of the tissue involved permits cell multiplication, as well as differentiation.

Just as the segmenting ovum divides itself into parts which we name germ layers, each of which has its special and exclusive share in developing the adult tissues, so does each of the three germ layers divide into parts, each part having its special and inclusive rôle; and these parts again subdivide until, after the final partition, the adult variety is produced. During all these changes there is no exchange of rôles. It will be profitable to let the phenomena pass before us in rapid review.

First, then, the ectoderm. This layer early separates into two parts, one to form the central nervous system, the second the epidermis; the nervous part thereafter never forms epidermal structures, the epidermal part never forms a nervous system. The central nervous system retains in part a simple epithelial character, but most of its walls become nervous tissue; its cells pass from the indifferent stage and become neuroglia cells or young nerve cells (neuroblasts). Neuroglia cells

never become anything else, and the nerve cells are always nerve cells to the end. The primitive epidermis forms a series of special sensory areas and the permanent epidermis. The sensory areas, which belong to the olfactory, auditory, and gustatory organs, soon become well defined and never produce any cell arrangements like those of the epidermis. This last, on the contrary, remains, as before stated, rich in undifferentiated cells, and gradually produces a great variety of structures. Most of these, namely, the hairs and glands, are small and very numerous, while a few, like the nails, enamel organs, and epithelium of the lips, are larger. No one of these special structures, however, converts itself into another. The basal layer of the general epidermis may perhaps preserve a true embryonic quality and have wide differential possibilities.

Next, as to the entoderm, which undergoes less differentiation than either of the other two germ layers, since over a large part of its extent it remains throughout life a simple epithelium with many cells very slightly modified in structure. Wherever in it specialization takes place, as in the tonsil, thymus, thyroid, esophagus, liver, or pancreas, each territory of cells keeps its characteristics and never assumes those of another territory.

Finally, as to the mesoderm, in which layer variety of differentiation attains its maximum. To follow the genesis of this variety is most instructive. The mesoderm is found very early to include, in vertebrate embryos, four kinds of cells, of which the most numerous are undifferentiated cells, the other three kinds being (1) endothelial cells of blood-vessels, (2) blood cells, (3) sexual cells. All of these are precociously specialized; they are few in number, yet they are probably the parents of all the cells which are produced of their kind throughout life. Our present knowledge does not permit us to speak with entire certainty, but the evidence is strongly in favor of the following three conceptions: (1) That all the endothelium of the blood-vessels of the adult is descended directly

from the endothelium of the first blood-vessels differentiated in the extra-embryonic portion of the germinal area. (2) That all the red blood corpuscles are descendants from the red blood cells of the blood islands of the area vasculosa. According to this view the blood-forming organs, as they are called, merely provide sites where the red cells can multiply, as, for instance, in the mammalian embryonic liver or in the adult marrow. (3) That the primitive sexual cells by their multiplication produce all the cells from which the genoblasts, or sexual elements proper, male and female, are evolved.

The future will decide the validity of these conceptions. They are very significant, because they assume that there are cells which form exclusive classes, and are characterized by a special combination of qualities, so that while they retain so much of the embryonic character as to have still the power of rapid multiplication, they yet are so specialized that they can only produce their like. If the three conceptions are established, we shall regard these three sorts of cells as almost the first to be fully differentiated. We shall also have to regard the vascular endothelium as distinct not only from the epithelial lining of the body cavity, but also from that of the lymphatic system. The immense importance of such a discovery, as bearing upon pathological researches and interpretations, is obvious.

The next important change in the mesoderm is the development of the main-body cavity, which the embryologist designates comprehensively as the cœlom. The cells, which lie next the body cavity and border it, assume an epithelial arrangement; this epithelial layer around the cœlom is properly named *mesothelium*, and the loose cells about it constitute the *mesenchyma*. We do not have, however, at first, a true differentiation of mesothelial and mesenchymal cells; all are undifferentiated, and we can readily demonstrate that the cells are interchangeable, differing during early stages by their positions in relation to one another and to the body cavity, but not differing in their essential structures or qualities. Thus we

find that the mesothelium constantly gives off cells which join the mesenchyma, and we find later that mesenchymal cells may take on an epithelial arrangement around any of the cavities—and there are many such—which arise within the mesenchyma itself in the course of further development.

But although difference of arrangement does not necessarily indicate differentiation of the cells it does affect the character of the differentiation which ensues. As every text-book states, the mesothelium gives rise to the striated muscles and to the epithelial portions of the entire genito-urinary tract, and is permanently retained, with slighter modifications, as the epithelium of the pericardium, pleuræ, and peritoneum. The mesenchyma produces an even greater variety, since it is the parent of not only all the connective and supporting tissue, but also of the lymphatic system.

I venture to turn aside for a moment to urge upon you the adoption of the term "mesothelium" as the correct designation for the epithelial lining of the cavities of the thorax and abdomen. It is literally the same epithelium in the four cavities, for they were originally one with a single continuous epithelium. It is well also in our nomenclature to recognize the important fact that the epithelium is radically, because genetically, distinct from the endothelium of the blood-vessels and lymphatics, and the application of the term "endothelium" to the covering of, for instance, the peritoneum, leads and can lead only to confused bad thinking. If mesothelium be employed as suggested, clearness will be gained.

Coming back now to the subject of the mesoderm, let us note that when a striated muscle fibre is produced a striated muscle fibre it always remains, and it never becomes anything else; the ovary never changes. In short, with the mesoderm, as with the ectoderm and entoderm, we see the fate of the cells once fixed to be thereafter unchangeable as to the kind of differentiation.

Our hasty review is worse than imperfect, yet is sufficient to impress upon us the great law that differentiation in any direc-

tion terminates the possibility of differentiation in any other direction. In accordance with this law we encounter no instances, either in normal or in pathological development, of the transformation of a cell of one kind of tissue into a cell of another kind of tissue, and further we encounter no instance of a differentiated cell being transformed back into an undifferentiated cell of the embryonic type with varied potentialities.

Thus far I have expressed myself somewhat as if there were two sharply defined conditions, the differentiated and the undifferentiated. To give such an impression would be to create error, since differentiation is a slowly progressive and wholly gradual change in the cell. We must look upon each step in the process of differentiation as establishing narrower limits for future changes. Thus, when in the spinal cord neuroblasts diverge from the glia cells, they are not specialized into different classes of neuroblasts; such specialization comes later. So in the mesenchyma, after the embryonic cells have changed and large numbers of them have become connective tissue cells, these last still are capable of various further differentiations, and may, therefore, be said to have been arrested in their development at a stage of partial differentiation. This quality of the connective tissue cells is, from the pathological standpoint, one of the most important facts known to us concerning the structure of the body.

Having now elaborated, as far as time permits, our conception of the nature of differentiation, let us turn to our third fundamental idea, which concerns the changes which succeed differentiation. These changes are very unlike the constructive changes which precede them, for they are destructive. They fall into three main groups: (1) Changes of direct cell death; (2) necrobiosis,* or indirect cell death, preceded by changes in cell structure; (3) hypertrophic degeneration, or indirect cell death, preceded by growth and structural change of the cell.

Of direct cell death no discussion is here necessary, for the

* It is a matter for regret that so awkward a term as "necrobiosis" should have become current.

fundamental idea, which I wish to emphasize, is that necrobiosis and hypertrophic degeneration are normal processes, which invariably occur in the normal body and play, in many cases, important rôles in the life history of the individual. Without necrobiosis and degeneration on a large scale, the normal round of human life would be impossible. It is singular that in treatises on normal anatomy and histology these two subjects are generally neglected, or at most appear only as matters of incidental reference. The force of tradition makes us apply these terms as if they corresponded exclusively to pathological conditions. This tradition might still prescribe our mental attitude, were it not that the studies of the last dozen years have made us familiar with the enormous extent, variety, and rapidity of the destructive degenerations which go on in the pregnant uterus of placental animals, a degeneration which takes place without affording a trace or a suggestion of any pathological modification whatsoever of the organ. To our inherited prejudices the uterine phenomena alluded to are startling, but their evidence before the tribunal of biology has settled the case in favor of the plea that hypertrophic degeneration is a normal factor in typical healthy development.

The normal and pathological changes associated with the death of cells, and consequently also of the tissues which are formed by cells, are so nearly identical that they may be combined in a single discussion. For the more convenient presentation of the subject the following table has been prepared. Concerning the table, little explanation is necessary. A few special points need mention. The distinction made between necrobiosis and degeneration corresponds to recognizable differences, but our present knowledge is insufficient to provide clear definitions for the two closely related types of indirect cell death. I feel much doubt as to the propriety of including atrophy in the table at all, since it seems to me that we ought perhaps not to regard atrophy as a phenomenon of a distinct class, but merely as a result of necrobiotic or degenerative alterations in cells and organs. Under the heading "Degenera-

tion" the division into "cytoplasmic" and "paraplasmic" takes us beyond our present knowledge, while the division "nuclear" is added rather to satisfy a biological conscience than to represent a part of our knowledge.

DEATH OF CELLS.

First. Causes of death.
- *A.* External to the organism:
  - (1) Physical (mechanical, chemical, thermal, etc.).
  - (2) Parasites.
- *B.* Changes in intercellular substances (probably primarily due to cells):
  - (1) Hypertrophy.
  - (2) Induration.
  - (3) Calcification.
  - (4) Amyloid degeneration (infiltration).
- *C.* Changes inherent in cells.

Second. Morphological changes of dying cells.
- *A.* Direct death of cells:
  - (1) Atrophy.
  - (2) Disintegration and resorption.
- *B.* Indirect death of cells:
  - (1) Necrobiosis (structural change precedes final death).
  - (2) Hypertrophic degeneration (growth and structural change often with nuclear proliferation precede final death).

Third. Removal of cells:
- *A.* By mechanical means (sloughing or shedding).
- *B.* By chemical means (solution).
- *C.* By phagocytes.

The preceding table represents the only attempt of the kind known to me, and like other first attempts is undoubtedly very imperfect. It embodies obviously no new facts. But, because it is frequently a scientific gain to systematize our information, I hope the table may be useful, and it will certainly serve its immediate purpose, namely, to guide our discussion of the normal changes which follow after cellular differentiation.

As the time at our command is brief, let us pass by the consideration of the causes of cell death. I will remark only that I think amyloid degeneration may be found to occur in the placental decidua of the human pregnant uterus and perhaps in other normal structures. No positive information on this

point is known to me. For the reasons stated a few minutes ago, atrophy may also be omitted here. We pass by also the direct forms of cell death, to reach at once the consideration of the indirect forms.

The accompanying table offers an analysis of some of the principal varieties of structural change which occur during indirect cell death.

INDIRECT DEATH OF CELLS.

A. Necrobiosis.
- (1) *Cytoplasmic changes:*
  - (*a*) Granulation.
  - (*b*) Hyaline transformation.
  - (*c*) Imbibition.
  - (*d*) Desiccation.
  - (*e*) Clasmatosis.
- (2) *Nuclear changes:*
  - (*a*) Karyorhexis.
  - (*b*) Karyolysis.

B. Hypertrophic degeneration.
- (1) *Cytoplasmic*:*
  - (*a*) Granular.
  - (*b*) Cornifying.
  - (*c*) Hyaline.
- (2) *Paraplasmic*:*
  - (*a*) Fatty.
  - (*b*) Pigmentary.
  - (*c*) Mucoid.
  - (*d*) Colloid, etc.
- (3) *Nuclear* (increase of chromatine).

We begin, therefore, with necrobiosis. We may appropriately mention first those organs of which the existence is limited in time, such as the thymus and the fetal kidney (mesonephros or Wolffian body). These organs attain first their full differentiation; their elements during the next phase die off, and finally are resorbed, most of the organ disappearing. In the same category of change belong the histories of the senile ovary and testis. Another familiar illustration is offered by

* I cannot venture to assert that these two divisions are valid, and not arbitrary.

the notochord, which in the mammals totally disappears during the fetal period. The notochord cells undergo peculiar characteristic modifications, hence it is difficult to say whether or not there is degeneration in the strict sense. Cell death on a large scale is a common phenomenon of the tissues. It occurs in cartilage, both when the cartilage is permanent and even more conspicuously when cartilage gives way to bone, the disintegration of the cartilage cells preceding the irruption of the bone-forming tissues. It occurs among the bone cells after they are imbedded in their calcified matrix. It occurs in the ovary, where we designate its result as atresia of the follicles. It occurs in the sebaceous glands as an accompaniment of the process of their secretion. It occurs among the glands of the intestine, as discovered by Stöhr, and occurs normally, though not constantly, in the appendix, as recorded by Ribbert. It occurs in the epithelium of the human pregnant uterus and in all the tissues of the human decidua reflexa. Other examples could be enumerated, but we may content ourselves with citing the constant destruction of blood corpuscles, both red and white.

Degeneration, in the stricter sense of an ante-mortem hypertrophic change of cell structure, is also of widespread occurrence in the healthy body. No case of so-called granular degeneration under strictly normal conditions is known to me, though it seems quite credible that such cases should occur. On the other hand, the cornifying degeneration is very important, and does occur in all three germ layers, for we observe it in the ectoderm of the skin, the entoderm of the esophagus, and the mesoderm of the vagina. Hyaline degeneration of so striking a character as to have been termed pseudo-pathological takes place regularly in the ectoderm (outer epithelium) of the placental chorion. In the rabbit it occurs in the uterine glands during pregnancy, causing most rapid histolysis, and it seems to me probable that some of the changes which can be observed in the decidua of the pregnant human uterus ought also to be regarded as cases of hyaline degeneration. That fatty degeneration takes place normally has long been taught. There

seems no reason for regarding the development of ordinary or mesenchymal fat cells otherwise than as instances of normal degeneration. In old age a more or less marked fatty degeneration may be widespread and occur in many different kinds of cells. The same is true of the deposit of pigment, as we see it in the liver cells and motor nerve cells of adults. Finally, mucoid and colloid degeneration are so obviously normal that we commonly think of their pathological occurrence as merely an exaggeration of a normal state.

The various kinds of changes in dying cells with which the pathologist is most familiar recur in healthy tissues. In the preceding table seven forms of change are enumerated under the heading "Necrobiosis." Every one of these seven occurs normally. Granulation of the bodies of the cartilage cells and of the notochord cells may be observed to precede their resorption. Hyaline transformation is conspicuous in the decidua reflexa. Imbibition or cellular œdema occurs in the epidermis of the lips, in the cells of the uterine glands during pregnancy, after they have detached themselves from the gland walls, and in the endothelium of the placental blood-vessels of the rabbit. Desiccation is the usual accompaniment of cornification. Clasmatosis has given its name to the clasmatocytes of Ranvier, and we may well apply the same term to the cells of the secreting milk gland, and also, as an unpublished research indicates, to the cells of the secreting glands of the cervix uteri. Karyolysis is, according to present probabilities, the method by which nucleated red blood cells are converted into non-nucleated blood corpuscles. Karyorhexis, or the fragmentation of the nucleus, occurs in the cells of the disappearing follicles of the ovary.

Lastly, as to the removal of cells. The sloughing off of cells is one of the most familiar phenomena, since it occurs incessantly over the epidermis and with the hairs; its part in menstruation and its colossal rôle in the after-birth are known to all, and every practitioner is accustomed to look for shed cells in urinary sediment. Large numbers of cells are lost by the

intestinal epithelium. Cells without access to the external world must be got rid of by resorption, which seems to take place either with or without the co-operation of leucocytes. In the latter case we must for lack of a better hypothesis attribute the resorption to chemical means. Of resorption with the aid of leucocytes the necrosed human decidua reflexa offers a perfect illustration. Of resorption without leucocytes the masses of degenerated epithelium in the placenta, periplacenta, and obplacenta of the rabbit afford by far the most impressive demonstration I have ever seen. At nine days after conception the epithelium is profoundly changed, being very much thickened, and where thickened transformed into a syncytium without cell boundaries, but with an enormously increased number of nuclei. In the obplacenta (or portion of the uterine wall opposite the placenta proper) a portion of the epithelium from the fundus of the glands remains, but the upper stratum has not only undergone syncytial degeneration, but has become vacuolated and partly resorbed without being directly attacked by either leucocytes or epithelium or any other kind of cells. At eleven days the resorption has progressed still further, so that the degenerated part is almost gone, but meanwhile the isolated patches of epithelium have spread until they united and so reformed a continuous epithelium. At thirteen days the epithelium has reconstituted new glands or follicles, very unlike, however, those of the resting uterus. To explain the extraordinary rapid disappearance of the degenerated material in the obplacenta, the only available hypothesis seems to be that of a chemical change by which the material becomes soluble or is dissolved, for we see the disappearance of the substance taking place in the very heart of the layer, and not merely at the surface. Sloughing is impossible, and there are no phagocytes, leaving the chemical explanation as the only one I have been able to conceive. The contemplation of the described phenomena of the rabbit's obplacenta inevitably raises the question—Do we not tend in our explanations of the removal of necrosed and degenerated tissues to attribute too much to

phagocytes and too little to direct chemical action? May it not be that the body produces histolytic toxins which can destroy tissues somewhat as do snake-poisons?

The cycle of changes through which cells pass is obviously longer than the period of development and the differentiation, yet its phases all belong together as members of a single series. We lack a word to designate the entire series of changes, and for the lack of such a word often fail to appreciate the essential unity of progressive and regressive modifications of cell-structure. Accordingly, I wish to propose the new term, "cytomorphosis," to designate comprehensively all the structural alterations which cells, or successive generations of cells, may undergo from the earliest undifferentiated stage to their final destruction.

Part II.—Pathological Differentiation.

We have now completed our brief reviews of the four fundamental successive stages of cytomorphosis. These stages are: (1) Undifferentiated; (2) progressive differentiation, which itself often comprises many successive stages; (3) regression (necrobiosis or degeneration); (4) removal of the dead material.

Let us now apply some of the conceptions won to the interpretation of pathological differentiation, remembering all the time that the interpretation of diseases is a distinct and different problem. Although presumably pathological differentiation is the sole and exclusive cause of disease, and no disease arises from any other immediate cause, yet the disease must be regarded as the result, and, owing to the physiological correlation of the organs, this result may include many secondary effects, some of which are often of the greatest diagnostic value, and therefore likely to divert attention from the primary structural cause.

Our review of normal conditions furnishes us with three general conceptions, which are valuable for their pathological applications, namely: (1) That each germ layer has a specific and

exclusive share in the production of tissues; (2) that undifferentiated cells, characterized by having only a small amount of unspecialized protoplasm, exist not only in the embryo, but also throughout life in certain parts of all three germ layers; (3) that differentiated cells, characterized by having a larger amount of specialized protoplasm, form most of the organs of the adult, and are incapable of undergoing any new unlike differentiation, though they are still capable of completing their cytomorphosis, by necrobiosis or degeneration.

We must apply these conceptions, according to my belief, as rigidly to pathological as to normal development. Thus, as to the germ layers, it ought to be possible, even with our present knowledge, to show their pathogenic values, so that every elementary student, as a matter of course, can be taught to classify accurately most pathological differentiations, and to accept such a classification as the basis of all his further study of the science. How much this reform is needed is indicated by the many writers who put glioma under the head of connective tissue tumors, although gliomata arise from the ectoderm, and connective tissue arises from the mesoderm. Such a classification is on a par with the ancient system which put the whales among the fish, for it is not going too far to say it is impossible that connective tissue should produce a glioma, because the two things belong in different classes. Another noteworthy violation of embryological law is offered by the classification of all muscle tumors under one head, "myoma," although smooth and striated muscle fibres are genetically and structurally distinct, with no intermediate or connecting forms of tissue, and with only a slight physiological resemblance. As regards epitheliomata, they should be studied in relation to their layership; and it is reasonable, in my judgment, to expect that they will be found to have very distinctive characteristics, according to the germ layer from which they take origin, for the layership of a tissue governs the normal differentiation and therefore probably also the abnormal. I believe that the first competent investigation in this field will mark a new epoch of

pathological science. When that epoch comes our morphological sense will no longer be shocked as, for instance, by the application of the name adenoma to an epithelioma of an organ like the kidney, which is in no sense a gland.

I should like to urge especially the study of the layership of the various cancers. Can we safely assume that there is only one kind of cancer? May it not well be that ectodermal, mesothelial, and entodermal cancers are separate kinds?

Next, as to undifferentiated cells. The cells of this sort have the power of multiplication in a high degree, and they have the possibilities of increasing their size and of undergoing further differentiation, and their occurrence in the adult is of the utmost pathological significance. Such cells exist in four important parts: (1) in the basal layer of the epidermis and in corresponding portions of the epidermal appendages; (2) in the adult mesenchyma or connective tissue; (3) in many parts of the adult mesothelium, especially of the epithelia of the genito-urinary tracts; (4) in the entodermal epithelium of the gastro-intestinal tract. It is significant that it is precisely from these parts that the development of many rapidly growing tumors takes place, and it is further significant that the least differentiated or specialized of all, namely, the mesenchymal cells, are the ones which produce the greatest variety of tumors, as the following list recalls: myxoma, myoma (but not rhabdomyoma), fibroma, lipoma, chondroma, osteoma, and sarcoma. Angioma presumably belongs in a different category. The mesenchyma still exhibits, by the formation of its characteristic tumors in the adult, its embryonic capacity to transform itself in varied ways.

Further insight into pathological development may be gained from the tissues or cells which have undergone differentiation but do not attain a high grade of specialization. The endothelium of blood-vessels, the endothelium of lymph vessels, the red blood cells, the leucocytes, and the neuroglia are examples of this class. All the cells of the kind just enumerated have advanced in organization beyond the embryonic state, but have

retained the power of cell multiplication. When they multiply they produce cells like themselves, so that we might describe them as so many histological species, each capable of reproducing its own kind. In accordance with this conception, derived from the normal development, is the pathological fact that each of these species of cells produces tumors of its own kind. This is a familiar conclusion as regards the endothelium, both of the blood-vessels and of the lymph vessels, and also as regards the neuroglia. It seems to me that the excessive multiplication of leucocytes may properly be classed in the same category as the growths resulting in angioma and glioma. I do not know whether or not an excessive and abnormally rapid production of red blood cells may occur so as to occasion a special and distinct disease. Increased production of red blood cells (erythrocytes) is, of course, well known to occur, but I understand that a distinct disease of this origin is, as yet at least, not recognized. It is not improbable, however, that such a disease exists — we should, I suppose, name it *erythrocytosis* or *hematoma*.

We can now distinguish two main groups of new formations: (1) those with marked cytomorphosis, or change in cell structure, as, for example, myoma, lipoma, chondroma, etc.; (2) those without marked cytomorphosis, the cells of the new growth resembling those of the parent tissue, as, for example, angioma and glioma. Members of the first group have been termed *heteroplastic*. Members of the second group have been termed *homoplastic*.

Accepting these terms we may say tumors are either *heteroplastic* or *homoplastic*. From the standpoint of the embryologist these terms are much more than convenient adjectives; on the contrary, they denote differences of a fundamental character, upon which we must base a large part of our notions about pathological differentiation.

Finally, as to the differentiated cells. We have just considered cells which have reached a low degree of differentiation and therefore will now give our attention only to the most

highly differentiated. Of these the nerve cells, or, as they are now termed, the neurones, stand highest, and are characterized not only by the great specialization of their organization, but also by the complete loss of their ability to multiply by cell-division. The neurones are then extremely unlike the embryonic cells, and they represent the extreme end of that scale of which the undifferentiated cell is the beginning. It is, therefore, very significant that neurones do not form tumors. Neuronoma, as such a tumor would be called, does not occur, so far as hitherto recorded, and if, as is possible, a neuronoma should be found, we should have to explain it not as a tumor-growth of neurones, but as the result of proliferation of indifferent cells, which subsequently became differentiated into neurones. The so-called neuromata of pathologists do not here come into consideration because they are merely accumulations of growing axis cylinders.

Liver cells and striated muscles also represent a very high differentiation. It is possible that with more exact knowledge we shall be able to state that these elements also cannot produce tumors, although there may be tumors of the liver and of striated muscle fibres. Possible, because Cohnheim's famous theory of tumor origin from persistent embryonic tissue may be, though not generally applicable, yet available in these two instances. The adoption of this view would furnish an explanation of several familiar facts: of the fact that we do not find tumors formed by differentiated liver cells; of the fact that cancer of the liver arises usually from the bile ducts, which have a simple and little differentiated epithelium; of the fact that myoma of the cardiac and of the developed skeletal muscles is exceedingly rare; of the fact that rhabdomyomas so occur that their origin may be attributed to inclusions of portions of embryonic muscle plates. As regards primary epithelioma of the liver, it is claimed that it arises usually from the bile ducts, but the liver cells are also involved; but how it comes about that the liver cells participate is, so far as I have been able to learn, by no means clear.

From analogy with other tissues, we infer that it is improbable that the large and specialized liver cells ever resume an embryonic character. In short, I deem our understanding of the pathological differentiation of hepatic cells and of striated muscle fibres too imperfect to support a judgment. We can only say that the rarity of such differentiation concords with the degree of normal specialization of the cells and fibres in question.

Our very brief discussion of pathological differentiation seems to justify the following conclusions: (1) The process in its essential features is identical with the process of normal differentiation; (2) the character of a tumor depends primarily upon the layership of the cells producing it; (3) normal differentiation impedes and limits the formation of tumors, precisely as it does of further normal structures, so that tumors arise most readily from undifferentiated tissues and may then be heteroplastic; arise less readily from differentiated tissues and are then always homoplastic; and arise unreadily or not at all from the most highly specialized tissues. Each of these three conclusions might be advanced as a law of normal development, if we substitute the term "differentiated tissue" for "tumor."

We now pass on to the final stages of cytomorphosis, necrobiosis, and hypertrophic degeneration, in their pathological manifestations. The consideration of the direct or simple death of cells need not detain us, nor need we pause long over the indirect forms of cell death. In fact, the analysis made earlier this evening of normal necrobiosis and degeneration forced us to recognize that all, or nearly all, the modes of indirect cell death which the pathologist encounters in morbid tissue recur under healthy normal conditions. To put the conclusion in its correct form, we need only to reverse it, saying: Most, and probably all, pathological necrobiosis and degenerations of cells are essentially identical with normal processes, and are pathological owing to the abnormality of their occurrence in time and site.

Death of a cell may, of course, occur at any moment as a consequence of conditions external to itself. To a given cell, as such, it is of no moment whether the term "physiological" or "pathological" be applied by us to the conditions which cause its death. The cell has its own inherent qualities, and its own cytomorphic possibilities. All that the environment of the cell can do, so far as we can at present understand, is to evoke, and perhaps to a minor degree modify, one of the possible structural changes of the cell. Hence we find actually that the processes of cellular necrobiosis appear to us identical in normal and pathological cases. This affirmation does not imply that a given cell has only one kind of possible necrobiosis before it. Quite otherwise, it being reasonable to believe that any one of several forms of necrobiosis, according to the circumstances, may ensue.

All that has just been said might be repeated in reference to hypertrophic degeneration. One of the investigations which is most needed at the present time, and which promises results of extreme interest and importance, is the investigation of necrobiotic and degenerative cytomorphosis, carried out as a research upon cell structures. At present we cannot discuss the subject except in terms the very vagueness of which is a mortifying confession of ignorance.

Time forbids the prolongation of the discussion. But, although a more detailed study is thus for the present excluded, we have nevertheless dealt with the subject with sufficient fulness, I hope, to convince you, if you were not already convinced, that the fundamental problems of pathology and embryology are alike, not only in being problems of cell life, but also in being similar and even identical problems of cell life. Widely as the two sciences differ, they rest on a common foundation.

To complete our subject it would be necessary to summarize our present knowledge as to the causes of cell differentiation. Physiological morphology is a new science; we have barely crossed its threshhold, and are not yet at home in it. To the

physician this new science promises to far surpass in practical importance even the bacteriology of our time, since it is not presumptuous to hope that when we understand the physiological factors, thermal, chemical stimulant, mechanical, and other, which bring about structure, which cause cytomorphosis—that then we can acquire control over cellular differentiation, and ultimately be able to prevent some of the most formidable diseases, over which we now have little or no power. The diseases which we may attack in the future in this way are diseases which may be designated as morphogenetic, because they are due to errors of morphological differentiation. At this vast topic it is quite impossible now to more than hint.

Here we may stop, not because all the great host of relations between embryology and pathology have been marshalled before us, but because enough of those relations have passed us in review to present a conclusive body of arguments. As we follow their march, we find ourselves led to the attack upon the problem of the causes of the specialization of cells, of histogenesis. To conquer this problem our only hope lies in the junction of all our forces.

Before closing, a personal word: First, of sincere thanks for the honor you have conferred upon me, both by your invitation and by your attention, and then a word to express the great diffidence with which I have undertaken to deal with pathological phenomena. A man of science ranks according to the number of details which he has mastered, and his ability to drill them into coherent battalions. By no such system of ranking can I hope to be included among pathologists. I offer, therefore, only the thoughts of an outsider, derived from the long pursuit of a cognate science. Such external suggestions, being independent to some degree of pathological tradition, may contribute to vivify the conception of the unity of the biological phenomena, and, therefore, of all forms of biological investigation. It will be a service rendered if my words recall the great truth that biology is not a congeries of sciences,

but a single science, which we artificially divide and subdivide until the parts are commensurate with our mental capacity. In the truest sense we are fellow-workers. Let us, therefore, work together.

CONGENITAL OCCLUSION OF THE DUODENUM.

LOUISE CORDES, M.D.

Abstract.

Congenital occlusion of the small intestine is said to occur oftenest in the duodenum. Reviewing the literature upon this subject, so far as it was at my disposal, I find reported fifty-six cases of stenosis and atresia of the duodenum, my own case making the fifty-seventh. The oldest case on record is one described in 1808 by Aubéry (*Med. Chir. Zeitung*, Salzburg, iv., 269).

Total occlusions are more common than stenoses. Many authors state that atresias of the duodenum are most frequent in the middle and lower portions of this section of the gut.

The causes which may lead to intestinal occlusion are numerous, some of the most important being:

(a) errors of development, (b) volvulus, (c) fœtal peritonitis, (d) ulceration, (e) pressure caused by new growths, (f) abnormally long persistence of the omphalo-mesenteric duct, (g) traction due to inguinal hernia, (h) circulatory anomalies (absence of arterial branches), and (i) embolism of the superior mesenteric artery.

Pressure of the head of the pancreas upon the duodenum is spoken of by both Serr and Felix Heyman, each of whom cites a case attributable to this cause. As for embolism of the superior mesenteric artery, Virchow believes this to be an exceedingly rare cause of intestinal occlusion and Kuttner shares his view. The old idea that amniotic bands may cause strangulation of the intestine was disproved by Kuttner.

Peritonitis may be primary or secondary; when primary it

is most often of syphilitic origin. The fact that the majority of infants in whom malformations of this nature are found were born prematurely is mentioned by Schottelius as evidence in favor of specific disease as a causative factor.

Volvulus, caused by a long mesentery and the occurrence probably of exaggerated peristalsis, in conjunction with those changes of position which the intestine undergoes during its various stages of development, is held to be a very frequent cause of intestinal occlusion. Markwald excludes volvulus as a cause of atresia when the occlusion occurs at about the middle of the descending limb of the duodenum, since twisting at this point is, he says, prevented by fixation of the gut by the peritoneum.

Occlusion of the duodenum is most frequently very near the opening of the common bile duct into the duodenum, either above it or below it. In only eight of the reported cases was a distinct cause for the occlusion found.

The case which I report in this paper is the only one of its kind on record in the New York Infirmary for Women and Children. The history is as follows:

Mary W., a healthy Irish woman, thirty-eight years old, gives a negative history; no data pointing to specific disease could be obtained; she has had no miscarriages, but has borne six children, four of whom are dead and two living.

The last child, a girl, was born on October 20th, full term, after a normal labor. The child presented no abnormalities externally, weighed 3200 grms., and was 49 cm. long.

Her face at birth looked old and wrinkled; she nursed with difficulty, but when fed on a milk mixture, she took this fairly well, but vomited at intervals, the vomitus consisting of yellow material resembling bile; meconium in considerable amount was passed at intervals. On the third day a drawn, pinched expression of the face was noted. The infant was found dead in bed on the fourth day, the nurse having administered a stimulant a half an hour before, observing no change in the child's condition at that time.

On October 24th, an autopsy seven hours post-mortem, and the following notes were made:

The body is poorly nourished, there are no skin lesions. The feet are extended, the toes flexed, the fingers are flexed upon the thumbs.

The umbilical cord is dry and still adherent.

Brain.—Normal, save for congestion of the vessels of the pia. The sinuses contain fluid blood.

Lungs.—No pleurisy. Left lower lobe is three-fourths solid—on section atelectasis. The left upper lobe and all the lobes of the right lung contain scattered areas of atelectasis. The bronchial lymph nodes are normal.

Heart.—Both auricles are distended with blood, the valves are normal, and the foramen ovale is open.

Liver.—Congested, but otherwise normal; the umbilical vein contains dark semi-fluid blood.

Spleen.—Has two lobes; it is somewhat congested and slightly enlarged.

Kidneys.—Are reddish-gray, showing fœtal lobulation. The capsules are free, the surface beneath is smooth. On section the cortex is normal and the markings are distinct. The tubules of the pyramids contain uric acid.

Pancreas and *adrenals* are normal, a small portion of the former lying flattened against the posterior wall of the dilated duodenum.

Œsophagus.—Normal. *Stomach* contracted with the exception of the pyloric ring, which has a diameter of 1½ cm. The stomach is larger than normal, the pyloric third having undergone considerable distension; the greater curvature measures 14½ cm., the lesser 6½ cm. The pylorus leads into a large oval sac which ends blindly just above the papilla; this sac in its greatest circumference measures 10 cm.; the inferior curvature from the pylorus to the obliterated portion measures 8½ cm., the superior 13 cm. The walls of the sac, like those of the stomach, are much hypertrophied, the mucosa is smooth, not showing valvular folds like those seen in the intestine below the atresia. The mucosa at the point of occlusion is smooth, showing no trace of cicatrization. On the postero-inferior wall of the blind sac there is an oval area about 5 mm. long and 3½ mm. wide in which the mucosa is lacking; at the point where the mucous membrane recommences it forms a straight valvular fold, beneath which is hidden the orifice of a canal about 4–5 mm.

long; a probe in this canal passes downward and inward issuing from the orifice of the common bile duct in the papilla.

The common bile duct is formed by the junction of the hepatic ducts, the pancreatic joining the main duct in the usual manner before the latter enters the duodenum. An accessory pancreatic duct is not present. The papilla is situated immediately below the atresia, which consists of a simple constriction of the gut at this point, the small intestine beginning as a blind sac below and having a diameter of 1½ cm.; the contents of the blind sac consist of a small amount of mucus and thin greenish-yellow fluid; the remainder of the small intestine is normal, its upper portion containing a little yellow, somewhat pasty material; the cecum and colon are normal, both containing meconium. The vermiform appendix and the mesenteric lymph nodes are normal, as are the peritoneum and peritoneal ligaments.

There is nowhere any evidence of inflammatory adhesions; the blood-vessels of the stomach and duodenum are much congested, but show a normal distribution.

The urinary bladder is contracted, and the uterus and adnexa are normal.

Anatomical Diagnosis.—Atelectasis; congenital atresia of the duodenum above the orifice of the ductus choledochus; hypertrophy and dilatation of the stomach and upper portion of the duodenum; general congestion.

Microscopic Examination.—The blood-vessels of the lung are congested, and the organ shows the lesion of atelectasis.

The spleen is much congested, the thymus body, kidneys, pancreas, and suprarenals are normal.

Stomach.—Save for considerable desquamation of the epithelium, the mucosa is normal. The muscular layers are thickened; the peritoneum is normal.

Upper dilated portion of the duodenum.—The mucosa and submucosa are thinner than the corresponding layers of the duodenum below the atresia, but their structure is normal. The epithelium lining Lieberkuehn's glands is desquamated in places. Compared with sections from the duodenum of a number of normal infants, the villi and the number and arrangement of Lieberkuehn's glands are apparently normal. Numerous groups of Brunner's glands are found in the submucosa and the peritoneum is normal, the endothelial

layer being in most places well preserved. Below the atresia the mucosa and sub-mucosa are well developed, and valvulæ conniventes are found. From a point 1 cm. below the papilla Brunner's glands become gradually fewer in number, ceasing 3–4 cm. below the atresia. Sections of the duodenum of infants at birth to eight to ten weeks old show the same arrangement and distribution of Brunner's glands. Transverse sections of the common duct at the papilla show a normal structure save for slight hypertrophy of the muscle coats. The tall columnar cells lining the duct have undergone considerable desquamation. The branch duct possesses the same structure as the common duct. Sections through the valvular fold which covered the orifice of the branch duct show it to be composed of a layer of connective tissue having the structure of submucosa; both surfaces of this layer are covered with a narrow mucous membrane—that on the superior surface possesses the structure of the membrane lining the duodenum, while that on the inferior surface resembles the lining membrane of the duct. Sections were made showing both papilla and duodenum, and these were compared with similar sections from the duodenum of normal infants at birth to a few weeks old; between the two there was a striking difference. The first showed few if any of Brunner's glands in the immediate neighborhood of the papilla, while in the latter the sub-mucosa in the same region contained an almost continuous layer of these glands.

In the case here described, there exists an anomaly of the common bile duct associated with atresia of the duodenum, no evidence of fœtal peritonitis, volvulus, old ulceration, or abnormal distribution of the arteries having been found. The presence of this branch duct explains one of the symptoms, namely, the vomiting of bile-stained fluid in spite of the position of the papilla below the occlusion.

Grouping the reported cases we find that females numbered 13, males 14, sex not stated in 30; 16 were premature infants: 1 born at seven months; 1, seven and one half months; 2, seven to eight months; 5, eight months; 1, eight and one half months; 8, premature (months not stated); 4 at term; 1, six weeks overtime(?); 36 not stated.

In the cases of total occlusion the ages varied from thirty hours to nine days; in the cases of stenosis from thirty hours to six months. Two, thirty hours; 1, thirty-eight hours; 1, forty hours; 2, two days; 1, two days and seventeen hours; 5, three days; 2, three to four days; 13, four days; 8, five days; 1, five days twenty hours; 3, six days; 2, seven days; 1, eight days; 1, nine days; 1, twelve days (stenosis); 2, first week; 9, not stated; 1, still-born; 1, six months (stenosis). The majority of the infants died on the third, fourth, and fifth days.

Vomiting was noted in 41 cases; vomiting not mentioned in 16; vomiting of material like meconium in 14; watery brown or yellowish material, 5; black or coffee ground or blood, 8; nourishment, 2; no mucus or bile, 2; nature of vomitus not stated, 10.

Meconium stools in 21; stools not stated in 29; stated no meconium, 6; blood in 1.

Position of the occlusion: above the orifice of the ductus choledochus in 20 (immediately above in 12; above but exact location not stated, 8); below the orifice of the ductus choledochus in 13 (immediately below, 2; below but exact location not stated, 11); on a level with the ductus choledochus in 2 (atresia in middle of duodenum); ductus choledochus opens into intermediate canal in 4; atresia near opening of ductus choledochus in 1; common duct not mentioned in 15 (first portion occluded, 3; at junction of duodenum and jejunum, 5; $3\frac{1}{2}$ cm. from pylorus, 1; 6 inches from pylorus, 1; duodenum ends blindly, 2; obliteration of lower portion, 1; complete closure of duodenum, 1; duodenum from pylorus to ductus choledochus converted into a cord, 1).

Contents of stomach not stated in 35 (*contents of duodenum above occlusion* not stated in 32; greenish material, 1; yellow frothy material or yellow fœces, 2); meconium or material resembling meconium, 7 (*contents of duodenum above occlusion* same as stomach in 4; not stated, 3); black material or brownish fluid in 7 (*contents of duodenum above occlusion* not stated,

4; same contents as stomach, 3); milk or other contents, 6 (*contents of duodenum above occlusion* same as stomach, 3; not noted, 2; brownish liquid, 1); glairy mucus, 1 (*contents of duodenum above the occlusion* not stated, 1); no contents, 1 (*contents of duodenum above occlusion* thin greenish-yellow fluid and a little mucus, 1). Contents of intestine below occlusion; not stated in 27; meconium, 15; stated no meconium in 1; pasty material or yellow fœces in 3; mucus or viscid material in 8; greenish-brown fluid with mucus, 1; red fluid, 1; empty, 1. Liver and pancreas: neither noted in 28; both normal in 10; liver normal in 9; pancreas, 2; pancreas not noted, 2; liver congested or large in 8; liver irregularly lobulated in 1; liver small and yellow absent in 1, gall-bladder absent in 1; small in 1.

In 49 cases no cause for the condition was demonstrated; in 8 cases fœtal peritonitis existed.

A number of facts, such as the repeated occurrence of duodenal occlusion near the site of the papilla, the existence, in probably more than one case, of anomalies of the duct system, the absence of Brunner's glands (in one case at least) at the point of and near the atresia, the striking absence of any signs of disease to which the condition might be traced, and the occurrence of other malformations than that of the duodenum in a certain number of the cases, lead me to think that an error of development not yet explained may underlie this condition.

It is much to be desired that in all cases of abnormality of the duodenum a careful search be made for the common duct and possible branches, microscopic examination following and sufficient data being given to allow of such a comparison of results as may lead toward a definite solution of the origin of this condition.

THROMBOSIS OF THE INFERIOR VENA CAVA.

O. H. SCHULTZE, M.D.

The specimen which I present this evening was taken from a woman, twenty-six years old, who had been admitted to the

City Hospital on January 18, 1901. The history has been furnished through the kindness of Dr. Thayer, pathologist of the hospital. On December 18th she had been delivered of a child by a midwife, and was said to have had fever and discharge for several days afterward. On February 4th, she complained of pain in the left knee and thigh. An examination of the blood on January 20th showed 11,250 white blood corpuscles and fifty-five per cent. of hæmoglobin. An examination of the urine showed it to have a specific gravity of 1.020 and to contain a distinct trace of albumin and many granular casts. On February 26th the blood gave a positive Widal reaction in a dilution of one to twenty. The temperature chart showed an irregular remittent type of fever. The autopsy had been held at the morgue forty-two hours after death. The immediate cause of death had been a fibro-purulent peritonitis involving the entire surface of the peritoneum. An abscess in the upper part of the spleen, evidently resulting from infarction, had infected the peritoneal cavity. A similar purulent infarct was found in the lower portion of the spleen. These infarcts were surrounded by marked connective-tissue proliferation. The fact that the infection of the peritoneum had not occurred earlier was probably to be explained by the presence of a very dense capsule. An organizing thrombus was found in the inferior vena cava, extending from the right auricle down throughout the entire inferior vena cava, and into both common iliacs and both external and internal iliacs. The wall of the inferior vena cava was enormously increased by connective-tissue proliferation. Both kidneys showed areas of anæmic infarcts surrounded by a small zone of inflammatory tissue. The uterus showed a marked thrombosis of all the veins with organization of the thrombi. The mitral valves showed an endocarditis verrucosa without purulent infiltration. In view of the Widal reaction having been present the intestine was carefully examined, but with negative result. Dr. Smith made cultures from the central portion of the spleen, from the two infarcts, from the contents of the gall-bladder,

and from a nodule on the mitral valve. Colon bacilli were present in all these localities, and bacillus pyocyaneus was isolated from the nodule on the mitral valve. In view of the time intervening before autopsy no reliable conclusions could be drawn from this examination. The case was remarkable in the entire absence of œdema and hemorrhagic infarction or any disturbance of circulation, with the exception of the anæmic infarcts of the kidneys and the pyæmic infarcts of the spleen. From the evidence of advanced organization of the thrombus in the inferior vena cava from below the entrance of the hepatic veins to the origin of the deep epigastric, and the venous plexus of the bladder, vagina, and rectum, this occlusion must have been of considerable duration. We must suppose that the anastomoses between the deep epigastric and internal mammary, the pelvic plexus, and the hemorrhoidal through the portal system, and finally the azygos veins, were sufficient to take care of the return flow.

Discussion.

Dr. T. C. Janeway: I have recently seen a man of fifty years of age with extreme dilatation of the superficial abdominal and thoracic veins, the current in them being upward. There had been apparent obliteration of the inferior vena cava. The patient was a physician who seemed to be perfectly well, and who stated that he had had this condition since childhood.

Dr. E. Libman: I have seen a case of suppuration of the left ovary and tube, with slight œdema of both lower extremities. Death had occurred rather suddenly, and the autopsy had revealed embolism of the pulmonary artery and thrombosis of the inferior vena cava. The thrombosis had begun in the left iliac and had extended almost up to the diaphragm. It seems to be the opinion of some authorities that the collateral circulation in these cases could be distinguished from that observed in portal thrombosis. In the latter there was more apt to be dilatation of the veins around the umbilicus, whereas in the

former the veins in the sides of the abdomen were enlarged. In a number of reported cases there had been no œdema of the lower extremities. The case cited by Dr. Janeway might also have been one of (congenital) stenosis of the hepatic vein at its junction with the vena cava.

Dr. E. K. Dunham: There is in the Harvard Museum a dissection showing congenital absence of the inferior vena cava with venous return through the azygos. This vessel emptied into the hepatic vein after it had left the liver.

A REPORT OF TWO CASES OF HYPERTROPHIC STENOSIS OF THE PYLORUS.

J. H. LARKIN, M.D.

Our knowledge of pyloric stenosis in infants dates back to the publication of Williamson in 1841. Another case was reported soon afterward, but it was not until the studies of Hirschbaum in 1888 that the subject attracted any great interest. Up to the present time forty-six cases have been reported; and to this list I am able to add another. Diagnosis of the condition intra vitam is unusual; in seven cases only was this done. Four were operated upon with one recovery.

The first specimen which I now present was taken from a child seven weeks old, weighing at birth 6¾ pounds. Nothing unusual was noted during the first two weeks of life, at the end of which time there developed frequent vomiting, persisting until death. No diagnosis was made. In this, as in all the other cases examined but two, there was found a hypertrophy of the circular muscular fibres of the pyloric ring. Microscopical examination of my case also showed a marked increase in the connective tissue between the muscular fibres. The tubular glands of the stomach were entirely replaced by connective tissue growth. My impression is that this is the first of its kind in which connective tissue new growth was a conspicuous feature. The second

specimen which I present was taken from an adult male, forty-six years of age. The musculature was entirely gone, being replaced by connective tissue. Of the theories offered to explain congenital pyloric stenosis two are worthy of consideration. One of these, the theory of Thompson, assumes that the stenosis results from an affection of the nerves supplying the muscles of the stomach. It has been contended that the change in muscular tone could not produce a muscular hypertrophy, and certainly that it could not account for the growth of connective tissue in the submucosa. The other theory presupposes the existence of an embryological defect.

Discussion.

Dr. SCHULTZE: I have also observed a case almost identical with the first one reported by Dr. Larkin. It occurred in a child dying at the end of six or seven weeks after birth. The vomiting had begun with the first nursing, and had continued persistently to the time of death. At the autopsy, the wall of the pylorus was thickened to 1 cm. The chief hypertrophy was in the circular muscular fibres.

A NOTE ON THE PROGNOSTIC VALUE OF THE DIAZO REACTION IN PHTHISIS.—PRIMARY ENDOTHELIOMA OF THE PERITONEUM.—PNEUMOCOCCUS TRICUSPID ENDOCARDITIS.

F. C. WOOD, M.D.

During the past year observations have been made at St. Luke's Hospital with the diazo reaction in two hundred and thirty cases of lung tuberculosis. Of these patients, one hundred and ninety are still living and present no diazo reaction. Ninety per cent. presented absolutely no reaction at any time, while the remaining ten per cent. occasionally showed a slight reaction. Some of these patients on becoming more severely

ill had developed the reaction. These results corresponded very closely with those obtained in certain German sanatoria. Of the fifty-two patients who died in the hospital, seventy-five per cent. gave a constant and strong reaction, and if the persons dying from nephritis or hemorrhage before the process in the lungs had become advanced were eliminated, the percentage of fatal cases giving the diazo reaction was ninety. Of those giving a strong reaction extending over several weeks, forty were fatal within three months. Fluctuations in the reaction were noted. For example, it had been repeatedly observed that in damp or rainy weather a much larger proportion gave the diazo reaction. The administration of any of the gallic-acid or tannic-acid preparations, as well as salol, creosote, and phenol, was followed by the elimination of a urine giving a similar reaction. No connection was observed between the degree of the reaction and the elevation of body temperature—in other words, the reaction seemed to indicate the extent of the tuberculous invasion of the lung rather than the amount of mixed infection. This test is being used in Germany as a basis for the exclusion of cases showing it from the climatic treatment in sanatoria.

The specimen of peritoneal endothelioma was taken from a woman of fifty-five, who had entered St. Luke's Hospital with a history of little else save emaciation and pain in the stomach. She was supposed to have a tuberculous peritonitis, and this diagnosis had been thought to have been confirmed by the laparotomy to which she was subjected. At the autopsy no growth could be found in the intestine. The gall-bladder was normal, and the lungs showed a few small metastases. As I have noticed an exactly similar condition result from the transplantation of colloid cyst adenoma to the peritoneum, a very careful search was made, particularly of the ovaries, for evidence of such new growth. Some hold that these growths are always primary in the intestinal mucosa; others that they originate in the lymph spaces of the subperitoneal lymphatics, but the

question is yet an open one. It should be remembered that the endothelia of the peritoneum and of the ovary are both developed from the mesoblast.

The pneumococcus endocarditis case was a woman of about thirty, who had entered the hospital with a serious lobar pneumonia on one side. Death had occurred in two or three days. Unfortunately no blood cultures had been made during life. At the autopsy both the tricuspid and mitral valves were found covered with small vegetations. They did not look like ordinary vegetations of malignant endocarditis, and the process did not seem to have invaded the valve substance deeply. Cultures from the vegetations showed the presence of pneumococci. The vessels in both lungs contained ante-mortem thrombi, but no infarction of the lung was present. The liver showed extreme fatty degeneration. The kidneys showed a moderate glomerular nephritis of a rather acute type. The appearance of the vegetations is quite characteristic of pneumococcus infection. The cases of endocarditis due to pneumococcus infection constitute twenty per cent. of all cases of malignant endocarditis.

Discussion.

Dr. James Ewing: I am much interested in the specimen of disseminated tumor of the peritoneum. It was almost identical in appearance with one presented to this Society a few years ago by Dr. Jeffries. At that time the view had been expressed that this was probably a primary tumor of the peritoneal endothelium. At the last meeting I presented some evidence against the view that these growths were endotheliomata. I found a small tumor of the intestine of a carcinomatous type that had produced a very small lesion of the intestinal mucosa and had rapidly reached the peritoneal coat, and was in process of spreading out and producing these small masses. This had led me to think that the old pathologists had been right in believing that this was an example of colloid

cancer secondarily involving the peritoneum. I do not think much could be learned from chemical examination of these cases. Without an extremely minute examination of the intestinal tract and of the pelvic organs as well, it is impossible for one to urge strongly that a given tumor originated from the endothelium of the peritoneum. Foreign authorities are strongly opposed to considering these as anything but growths of the intestinal epithelium.

Dr. J. H. LARKIN: I have always looked upon these tumors as carcinomata. On microscopical examination they seem to have a very close relation with the intestinal epithelium. About two months ago I studied a case in which the peritoneum had been covered with myriads of gelatinous tumors. After prolonged search I found the gall-bladder immensely thickened and holding four stones; and there was also one single metastasis into the liver of an adenomatous formation. The tumors in the peritoneum were gelatinous, just like those presented this evening. I believe in classifying these as carcinomata.

Dr. WOOD: Dr. Ewing does not seem to take into consideration certain recent reports from Germany. A search of the literature shows that it is almost the rule for the authorities there to take the ground that these tumors originate in the endothelium of the lymph spaces. The case under discussion gives no definite evidence as to its origin.

PRECIPITATION OF CERTAIN PROTEIDS BY BACTERIA.

E. LIBMAN, M.D.

The series of culture tubes and plates are presented to demonstrate the fact that many bacteria induce proteid precipitation in the presence of sugar serum or sugar albumen. Evidence of this may be easily seen by the whitening of the medium. Different bacteria induce various degrees of precipitation. Different degrees of precipitation occur in the

presence of different sugars. With one-tenth per cent. glucose no precipitation ordinarily takes place with the staphylococci. The typhoid bacillus usually does not induce this in the presence of lactose in any strength. Certain peptonizing organisms in the presence of glucose do not liquify gelatin.

It has also been found that the addition of one-half per cent. glucose to serum agar facilitates the cultivation of the gonococcus.

My studies in this direction suggest possibilities which may have considerable practical application, especially in the differentiation of bacterial species.

Proceedings

of the

New York Pathological Society.

NEW SERIES, Vol. I. May, 1901. No. 4.

TABLE OF CONTENTS.

LARTIGAU, Primary Sarcoma of the Thyroid Gland.—WILLIAMS, The Morphology of the Diphtheria Bacillus.—WOOD, Observations on the Staining of Malarial Organisms.—LE WALD, Syphilitic Ulcers of the Larynx.—WILSON, A Report of Two Cases of Gonococcal Endocarditis.—CONNER, Report of a Case of Abdominal Aneurism Rupturing into Right Pleural Cavity.

DR. EDWARD K. DUNHAM, *President.*

PRIMARY SARCOMA OF THE THYROID GLAND.*

AUGUST JEROME LARTIGAU, M.D.

The history of abnormal conditions of the thyroid gland begins several centuries ago. Although traces of naïve knowledge of enlargements of the thyroid body, and indeed of true sarcoma of this organ, also date back many years, a close study of the literature bearing on thyroid tumors has brought to light astonishingly few cases of sarcoma, especially of primary sarcoma. From the earliest publication of Alibert, in 1817, the subject passes unnoticed save the three cases reported by Raynaud, Forster, and Virchow, until 1870, when our knowledge of the subject was very materially advanced by Kaufmann. The basis of this observer's study was seven collected cases, three of which he had observed and examined himself.

The later literature has been enriched by other cases, reported from time to time mainly by Continental writers. Thus,

* For the complete article, see *Am. Jour. of Med. Sci.*, August, 1901.

Morf, after a critical search through the literature in 1899, was able to collect, including his own case, only forty examples of this uncommon disease. To this number I have been able to add fifteen others not included in Morf's paper, thus making a total of fifty-five recorded cases. It is only fair to point out, however, that these figures indicate too great an infrequency. Later statistical investigations will undoubtedly show that primary sarcoma of the thyroid gland is much more common.

The case which is the subject of this paper was clinically observed in the service of Professor Weir at the Roosevelt Hospital, and later came into my hands for autopsy. The salient points bearing on the clinical and anatomical features alone shall be given. The following are some of the main features excerpted from the history protocol:

J. M., a married woman, aged forty-five years, born in Scotland, was admitted into the hospital, January 3, 1901, complaining of a small mass in the neck. The family history is negative as regards tumors, syphilis, or tuberculosis. Ten weeks before present admission into the hospital the patient had been sick with pneumonia; otherwise she had always considered herself a strong and healthy woman. About eight years ago the patient noticed a lump in the middle of her neck at its lower part. It grew very slowly until it reached the size of a small hen's egg. This maximum was attained in about one year. At no time did it interfere either with breathing or swallowing. The patient considered herself quite well until ten days ago, when there appeared within two days a small lump on the right side of the neck, just above the middle of the clavicle. Since reaching maximum size on the second day the swelling has remained the same size. On pressure the parts were quite tender. With the appearance of this swelling there developed dyspnœa and dysphagia, which have become more and more severe. There had been no loss of flesh or strength; appetite remained good.

Physical Examination.– Patient is a well-nourished woman, whose breathing is labored and stridulous in character, and there is some loss of voice without hoarseness. In the median line of

the neck in the region of the thyroid there is a distinct tumor mass. It extends to the left of the median line one and one half inches, and tracheal rings can be felt beyond the left border of the growth, which is about the size of an orange. The growth is firm and elastic to the feel. Its outline can be fairly well made out, and it appears smooth and rounded. It is not painful on pressure. The overlying skin is freely movable; with deglutition the mass moves up and down, otherwise it appears more or less fixed to the deeper structures. The smaller mass, to which the patient particularly drew attention, is situated on the right side of the neck one inch above the clavicle near its middle. It is about the size of a walnut, somewhat firm, and very tender. The overlying skin is discolored blue. No enlarged lymph nodes are detected anywhere. The temperature on admission was 99.2°, and the urine contained a trace of albumen, but no casts were observed; the specific gravity was 1018. The operation for removal was performed by Dr. Brewer on the day following admission. Without mentioning the technical details of the surgical procedure, it may be said that the walnut-sized swelling just above the right clavicle was shown to be a hæmatoma located beneath the platysma muscle. The main tumor in the mid-neck was found to be encapsulated and not adherent to the anterior structures. The tumor was smooth, apparently cystic in character, and had replaced the right lobe of the thyroid. The isthmus and left lobe looked normal, and were not removed. Considerable trouble was experienced by the operator from the free hemorrhage which occurred in the incised tissues. No enlarged lymph nodes were observed during the operation. For about one week the patient's condition remained satisfactory, but after that it became increasingly worse from the dyspnœa, which became more and more severe owing to the actively recurrent growth which pressed more and more upon the trachea. Further, the amount of urine passed ranged only from eight to twelve ounces daily. On the sixteenth day after operation moderate ptosis of the right eye was observed. Two days later the right pupil was contracted, the left remaining normal. Toward evening general convulsions developed, and the patient died in full consciousness a little later, apparently from asphyxia.

The temperature, which had been 99.2° on admission, never

reached normal, but fluctuated irregularly, with an evening rise of 1° to 2° until death.

Description of Tumor Removed at Operation.—This has the size and contour of a goose egg (7 x 5 x 4 cm.). It is uniformly firm in consistence. The whole mass, which consists of the entire right lobe of the thyroid, is sharply encapsulated by a firm fibrous capsule from 1 to 2 mm. in thickness. Attached to the exterior of the latter are several torn fibrous adhesions. On section the cut surface is for the most part smooth, having a dark red color in some places, but for the greater portion showing irregular but sharply defined tissue of a yellowish or grayish color, extending from the interior of the encapsulating fibrous tissue in the form of strands, or in less definite forms, as though the tumor-infiltration occurred along the connective-tissue framework of the organ. Intermingled with this tissue, which is the tumor proper, is a considerable quantity of fresh and partly clotted blood. At one extremity of the specimen is a cavity about the size of a marble (2 cm.), which also contains clotted blood.

Histological Study of the Tumor.—Practically the whole of the normal thyroid tissue has been replaced by tumor growth. The fibrous-tissue capsule of the specimen for the most part is made up of dense fibrous tissue, but on one side (left) small portions may be seen in which new growth, similar to that of the main tumor, has occurred. At only one portion was invasion throughout the entire thickness of the capsule noted.

The portions of the thyroidal tissue which remained uninvolved by new growth showed changes, partly the result of compression. The alveoli of the gland are irregularly distorted into various shapes, from large oval or round spaces into mere slits in the tissue, containing some colloid finely granular material and extravasated red corpuscles. The epithelium, although sometimes normal in appearance, is largely compressed or else has completely disappeared. The fibrous-tissue framework of the thyroid adjoining the definitely involved portions shows an abundant round, oval, and spindle-cell infiltration, indicating the probable mode of extension of the growth along this portion of the organ.

For the most part the tumor consists of extremely cellular tissue containing numerous larger and smaller blood channels

filled with blood. The latter are more or less regularly distributed through the cellular tissue, usually separated from it by a sharply defined layer of endothelium. Occasionally, however, they appear to be mere blood spaces lying between the cells of the tumor without any intervening endothelial wall. Here and there within the blood vessels may be seen large masses of closely packed cells, often almost occluding the vessel lumen. They are similar to those making up the main tissue of the specimen.

The cellular portion proper of the tumor is made up of closely packed larger and smaller cells, whose nuclei take the nuclear dyes strongly. In morphology they conform to the spindle and small and large round-cell variety, with scanty cytoplasm. The spindle-cells predominate. Beside the former cell types a moderate number of cells of intermediate forms are likewise distributed among the main cell types. Occasional mitotic figures are made out, showing evidences of both regular and irregular division of the nucleus. The intercellular connective-tissue reticulum is observed only in places and is small in amount. Throughout the tissue between the cells may be seen red-blood corpuscles, extremely abundant in some portions of the tissue.

Histological Diagnosis.—Angiosarcoma (mixed cells) of the thyroid. The autopsy was made twenty-three hours after death. The brain was not examined, a partial autopsy only having been permitted.

Anatomical Diagnosis.—Primary sarcoma of the thyroid body, with well-marked reduction of the tracheal and œsophageal lumina by the pressure of the new growth; fatty degeneration of the heart; chronic diffuse nephritis; fatty liver; intramural nodular fibromyoma of the body of uterus; fibroadenoma of left breast; œdema and congestion of both lungs.

The incision wound in the neck was filled with granulation tissue and clotted blood. The remaining left lobe of the thyroid and isthmus were converted into a tumor mass irregularly oval in form. The whole mass measured 10 x 6 x 4 cm. It was sharply differentiated from the normal structures of the parts and limited above by the cricoid cartilage and extending downward to just above the clavicle. It reached outward to the right as far as the anterior border of the trapezius muscle; across to the left a little beyond the middle line of the neck, forcing the trachea over to

the right side. The trachea was compressed from the front and the left toward the right and backward. The lumen was not completely occluded at any point, but was much narrowed. Thus, at the third ring it measured only 4 mm. in diameter. The œsophagus at a corresponding place was also compressed from the front and the left. The large blood vessels of the neck were normal in appearance, although displaced well to the left side. On section the cut surface of the new growth presented a dark red appearance, mottled with small, irregularly sized areas of yellow and gray. There was no distinct evidence of encapsulation. Beyond recurrence at local seat, no metastases were found anywhere in the body, although these were searched for with great care, especially in the neighboring tissues, lungs, and bone-marrow.

The microscopical findings of the viscera confirmed the gross anatomical diagnosis. The histological features of the remaining left lobe and isthmus, which were found involved by new growth, were essentially the same as those already described in connection with the tissue removed at operation.

The bacteriological examination revealed the presence of the colon bacillus throughout the body. No clinical significance was attached to its presence, since it was regarded as the result of post-mortem invasion.

To summarize, then, this case is one of angiosarcoma developing in a goitre and pressing upon the trachea, causing death by asphyxiation. No metastatic growths were found anywhere beyond the local seat of the primary lesion.

ANALYSIS OF FIFTY-ONE CASES WITH REFERENCE TO PREVIOUS GOITRE.

Age-period.	Number.	Previous goitre.		No previous goitre.	
		Males.	Females.	Males.	Females.
10 to 20 years	1	1	0	0	0
20 " 30 "	3	1	1	1	0
30 " 40 "	5	1	1	3	0
40 " 50 "	14	5	8	1	0
50 " 60 "	18	6	8	2	2
60 " 70 "	10	2	1	4	3
Total	51	16	19	11	5

An analysis of a series of fifty-one cases of primary sarcoma of the thyroid shows that in thirty-five previous goitre existed, and in only sixteen was it absent. The incidence of thyroid sarcoma at different age-periods is not without some interest. Of eight cases which developed between the ages of twenty to forty, one half only showed previous goitre, while in a series of thirty-two others in which the sarcoma developed between the ages of forty to sixty so many as twenty-seven, or 84 per cent., had had goitre before the development of the sarcoma. This, then, indicates clearly enough that with the increase in age of these cases previous goitre becomes more frequent. With regard to its occurrence in the two sexes, it may be said that goitre seems to be more frequent in women; thus, it was present in 59 per cent. of the men and in 79 per cent. of the women.

That sarcoma of the thyroid occurs more frequently in advanced than in early life is a point on which all observers agree. The large majority of them occur after the fortieth year, with comparatively the largest number during the fifth decade.

For the entire fifty-three cases collected in the literature, the greatest number occurred between the years forty to seventy. To this age-period forty-five of the cases belong, while only ten of the fifty-five developed in persons under forty years of age. The earliest age at which primary sarcoma of the thyroid was noted was in a boy aged eleven years. For reasons which are not very apparent the greatest number of cases occurs between forty and sixty.

The relation of the origin of the tumor to the anatomical distribution is variable, but in the majority of cases, whether in men or women, the sarcoma originates in the right lobe of the thyroid gland. In forty-six cases in which this lobe distribution is noted, thirty-one, or 86 per cent., originated in the right lobe, and only fifteen, or 32 per cent., in the left lobe. The origin according to sex is as follows:

Sex.	Right Lobe.	Left Lobe.
Males (25).....	19 = 76 per cent.	6 = 24 per cent.
Females (21).....	12 = 57 per cent.	9 = 43 per cent.

From this table it may be clearly seen that the relative frequency of right- and left-lobe origin of the tumor is somewhat different in the two sexes. Thus, in man the right lobe was involved in 76 per cent. of the men and in 57 per cent. of the women, showing a comparatively much higher right lobe distribution in men.

Sarcomata of the thyroid ordinarily grow quite rapidly. The duration of the disease varies from several weeks to over one year. Lücke states that the course of the disease is usually less than one year; perhaps eight months represent the average. Death is often induced by involvement of the trachea or œsophagus, or both.

Conclusions. — 1. Primary sarcoma of the thyroid gland is rare, but probably of more common occurrence than statistics show. It is less frequent than primary carcinoma of the thyroid gland.

2. It is commonly associated with goitre. Those cases developing in persons between forty and sixty years of age show a higher percentage of previous goitre than younger individuals. Goitre associated with sarcoma of the thyroid is more common in women than in men.

3. Sarcoma of the thyroid occurs oftener in late than in early life. The greatest age-frequency is between forty and sixty.

4. Sex is probably an unimportant element in its development.

5. The primary tumor most frequently originates in the right lobe of the thyroid body. This distribution seems to be more frequent in men than in women.

6. The clinical course of the disease is usually relatively acute.

7. Involvement by pressure or new growth of the trachea or larynx is common.

8. Metastasis occurs through blood or lymph channels, or both.

9. Round and spindle or mixed celled sarcomata are most common. Angiosarcomata are not rare.

THE MORPHOLOGY OF THE DIPHTHERIA BACILLUS.

ANNA WESSELS WILLIAMS, M.D.

This investigation is based upon the study of forty pure cultures, which were isolated from a series of throat cultures showing in smears, besides the ordinary throat bacteria, suspicious or diphtheria-like bacilli only. There were frequently only a few of these bacilli present, and at first it was found difficult to isolate them, both because they were so few and because, as it later developed, those varieties of the diphtheria bacillus which appear oftenest in a typical form do not grow well upon agar when first isolated. It was found, however, that all varieties grow very well in ascitic broth even in the presence of other bacteria, and generally form a decided pellicle in twenty-four hours. After this fact had been demonstrated, ascitic broth was used in helping to isolate the few atypical bacilli. After making agar plates from such a culture a mixture of the whole culture was put into a tube of ascitic broth. From the pellicle which formed in twenty-four hours new agar plates were prepared. Within twenty-four hours these sometimes contained almost pure cultures of the diphtheria bacillus, and nearly always there were many isolated colonies.

The pure cultures, all of which were virulent, producing the specific toxin, were studied on seven different culture media; and it was found that in each culture, while there was great variation among the individual bacilli, certain morphological characteristics predominated, and that these remained fairly constant for a number of culture generations, and also in successive cultures taken from the same case when similar culture media were used and cultures of the same age examined. It was furthermore found that though each culture showed these individual characteristics, yet, when the characteristics of all were compared, two broad groups could be recognized in which those cultures having the distinct characteristics of the one group differed widely from

those having the distinct characteristics of the other, while between these extremes there were many gradations in type. The cultures placed at the two extremes differed from each other in the following general particulars: The first four showed most distinctly on two per cent. peptone agar after two days' growth; predominating bacilli in cultures at the one extreme were very large and showed large Indian-clubbed ends and decided branches. They were composed of many segments, and contained many metachromatic granules, more or less irregularly placed and divided according to the position of these granules; they grew moderately slowly and scantily, and surface colonies macroscopically were small and delicate and microscopically were small, coarsely granular, and non-spreading, with little or no central heaping. In alkaline two per cent. peptone broth they grew slowly and scantily, generally in tiny grains which formed a more or less dense precipitate, and they produced slight if any cloudiness and no pellicle. On the other hand, characteristic bacilli in cultures of the second group were small, had only occasionally small Indian-clubbed ends, showed fewer and smaller branches, and slight, if any, segmentation, and few granules, more or less regularly placed, one at either pole or both, or near the middle of the bacillus or in all three positions. They divided more regularly according to the position of these granules. Surface colonies macroscopically were moderately large and thick, and microscopically were large, more finely granular, and spreading with central heaping; in alkaline two per cent. peptone broth they grew rapidly and abundantly, clouding the broth and producing an abundant flaky, pellicle and precipitate in twenty-four hours.

A practical application might be made of the fact that there is a permanence of the predominating types in each culture from the same case, in helping to trace sources of infection. Another practical point is that when typical bacilli persist in a patient after convalescence from an attack of well-marked and characteristic diphtheria, there is very little need of testing the virulence of such bacilli.

Discussion.

Dr. LARTIGAU: Has Dr. Williams noted whether there was any definite relation between the different morphological forms and the virulence of the organisms studied?

Dr. WILLIAMS: All of the branched forms tested for toxin production had been found fully virulent. The bacilli which were the most virulent had the largest number of branches and segments.

Dr. E. K. DUNHAM: I have been struck with the fact that in this ascitic bouillon a medium has been found which seems to greatly favor the reproduction of the diphtheria bacillus, just as peptone favors the growth of the comma bacillus. Observations on development might vary a good deal in their results, depending upon the culture media used.

OBSERVATIONS UPON THE STAINING OF MALARIAL ORGANISMS.

F. C. WOOD, M.D.

Various combinations of eosin and methylene blue have been employed for staining the chromatin of the malarial organism. The original methods have been considerably modified; among these modifications that of Goldhorn * is the most recent. Specimens stained by this method show a peculiar granular staining of the red cells, especially those infected with the parasite. This has been assumed to represent granular degeneration of the cytoplasm of the red corpuscles. The significance of this appearance is, however, doubtful. According to my experience this granular appearance observed after the use of Goldhorn's stain is probably often due to artifacts resulting from the precipitation of substances within the cells. Similar changes have previously been noted in the blood of malarial patients, the so-called "tüpfelig" cells of students of tropical malaria.

* Goldhorn, *Proceedings of the New York Pathological Society*, 1901. New Series, Vol. i., No. 1, p. 7.

By the method of Goldhorn a precipitate is formed in the red cell and it is this which gives rise to these small granules. If the specimen be treated for an instant with alcohol, all of these granules may be washed out of the single cells, while they will remain just where two cells overlap, because here the alcohol does not penetrate so quickly. I have also found that the granules may be obtained very easily in normal blood. They are not especially abundant in the blood of rabbits, in which injections of pyrodin or lead acetate has caused all stages of true granular degeneration.

Discussion.

Dr. JAMES EWING: When I first looked at specimens stained by Goldhorn I then assumed that these granules were due to a precipitate. Since that time I have come to the conclusion that the Goldhorn stain brings out the true granular degeneration of the red cells somewhat better than other methods. I also found, as Dr. Wood did, that it was difficult to wash out the granules in cells which overlap, but I finally decided that these were not artefacts, because of their uniform presence in cells infected by parasites, even when fixed by other methods. The mere fact that they disappear under the action of such a general solvent as alcohol is not a sufficient reason for assuming that they result from a precipitate. These particles are not crystalline, but granular. There is certainly great danger of mistaking artefacts in the red cell for true granular degeneration. Many such seem to be dependent for their formation upon too short a period of fixation.

Dr. WOOD: The chromatin remains stained for a considerable time after treatment with alcohol, although all of the granules disappear. The infected red cells stained by Goldhorn's method are practically all granular, which is far from being the case if they are stained by almost any other method intended to bring out this granular degeneration. If the specimens are fixed in alcohol for half an hour or more the granules are not so likely to be present.

SYPHILITIC ULCERS OF THE LARYNX.

L. LE WALD, M.D.

This case is interesting on account of the fatal issue. The specimen shows a ragged ulcer measuring 3 x 1 cm. on the anterior aspect of the larynx in the region of the cricoid cartilage. There is considerable infiltration about it. There is a second ulceration measuring 4 x 2 cm. on the lateral aspects of the larynx, about the thyroid cartilage, below the vocal cords. This also presents a ragged, irregular centre and grayish borders. The patient was a woman, thirty-six years of age, who had been brought to Bellevue Hospital suffering from intense dyspnœa. She was unconscious at the time of admission, and a hasty tracheotomy had been done through the third ring of the trachea. Death occurred about two hours later. A diagnosis of probable syphilitic ulcers of the larynx was made by the house-surgeon, although no opportunity had been afforded for a laryngoscopic examination. At the autopsy there was a moderate œdema of the larynx in the region of the arytenoid cartilages, and the heart was dilated and very flabby. Apparently death had resulted chiefly from the dilatation of the heart, the latter having been dependent more upon the prolonged dyspnœa than immediately upon asphyxiation. Sections of the lower ulcer showed a superficial necrosis and a round-cell infiltration in the deep tissues. There was no evidence of tuberculosis here or elsewhere in the body. The lymph nodes generally showed a hyperplasia apparently of syphilitic nature.

A REPORT OF TWO CASES OF GONOCOCCAL ENDOCARDITIS.

R. J. WILSON, M.D.

These cases are especially interesting because of the fact that apparently only three have been reported in which the

gonococcus has been recovered from the blood before the death of the patient. Before the recovery of these organisms from the blood there had been no suspicion of the presence of the gonococcus. The cases occurred in the First Medical Division of Bellevue Hospital. The first blood cultures were made on December 18, 1900, three bouillon cultures being made in tubes containing about 3 c.c. The blood was taken from a superficial vein on the outer surface of the left wrist. The cultures were incubated at 33° C. and examined at the end of twenty-four hours. At this time no appreciable growth in the broth was noted. At the end of forty-eight hours no change occurred in the bouillon, but the plates showed small, delicate surface colonies, looking to the naked eye like minute drops of serum. Having no idea of what the colonies were, Loeffler's blood serum was selected as the medium for culture. Of the new cultures, only one developed organisms, and here the growth was very scanty. New cultures were made in other blood-serum tubes, and from these further experiments were made. The cultures were made in the ordinary nutrient bouillon and on agar, and, with one exception, they failed to develop. A smear made from the original colony gave a diplococcus which stained irregularly with methylene blue. On December 28th, or ten days later, cultures were again taken from the blood. One cubic centimeter of blood had been obtained, but no growth developed. The patient died on the following day. The autopsy showed vegetations on the heart valves, and a double pyosalpinx. Sections of the vegetations showed numerous diplococci identical with those found in the blood cultures.

The second case occurred on March 10, 1901, and cultures were made with 1½ c.c. of blood. One half of the specimens were cultivated anaerobically, and the others in the ordinary way. Nothing developed. On March 23d, cultures from this case were again made, using glucose agar. This time four colonies developed on one plate, but in transferring them they became contaminated. On April 1st, another series of

cultures were made. At the end of twenty-four hours' incubation nothing was visible. At the end of forty-eight hours, one agar plate and one glucose agar plate showed colonies resembling those found in the first case. They were transferred to Loeffler's serum. The urine was then centrifugalized, and in the sediment a diplococcus was found which was apparently identical with that isolated from the blood. I attempted to cultivate these organisms, but failed to get pure cultures.

Discussion.

Dr. G. LANGMANN: Which valves of the heart were involved in these cases? I know of two cases of malignant endocarditis reported by Dr. I. Adler, in which the presence of the gonococcus had been proved. In each case the tricuspid valve had been involved, and I am under the impression that Dr. Adler stated at the time that he had noticed that the gonococcus exhibited a predilection for this valve.

Dr. A. J. LARTIGAU: It is interesting that Dr. Wilson is willing to accept these cases as gonococcal in origin. As to the distribution of the lesion in that class of heart infection, I cannot agree with Dr. Langmann's statement. I have recently analyzed a series of fifteen fairly conclusive cases, and found that the mitral valve alone had been involved three times, the aortic eight times, and both valves of the left heart twice. The tricuspid was found to have been involved but once and the pulmonary twice.

Dr. F. C. WOOD: In cases due to the pneumococcus the right side of the heart is more commonly affected.

Dr. CHARLES NORRIS: The bacteriological evidence offered by Dr. Wilson does not seem to me to be conclusive of the gonococcic nature of the endocarditis in these two cases.

Dr. WILSON: The organism would not grow on ordinary media, and was identical in its cultural and staining peculiarities with the one isolated in the first case, which had been controlled by fifteen gonococcus cultures. The proof is not

quite conclusive, it is true; I had no opportunity of cultivating the organisms from the urine. No bacteriological examination was made of the double pyosalpinx.

Dr. E. LIBMANN: If use of serum-glucose agar be made as suggested by me, one must be careful, before making a positive diagnosis, of colonies being those of the gonococcus. For while there is a better chance of obtaining colonies in this medium, some bacteria that are usually not decolorized in the Gram procedure may become decolorized, probably due to the acid production. Furthermore, the acid production may decrease the vitality of the organism so that it will not grow at all, or at least not on the ordinary media. This is mainly true if one wait too long before transplanting the colonies. Careful attention to the morphology and to the reaction to the Gram stain in media not containing sugars is therefore necessary.

REPORT OF A CASE OF ABDOMINAL ANEURISM RUPTURING INTO THE RIGHT PLEURAL CAVITY.

LEWIS A. CONNER, M.D.

The specimens were taken from a man thirty-four years of age, a fisherman, who had given no certain history of syphilis. For five months he had had moderate epigastric pain. On April 26th he had been suddenly seized with severe epigastric pain and syncope, and had been brought in the ambulance to the Hudson Street Hospital. I saw him within an hour, and found him in collapse. There was a prominence of the epigastrium and a fairly distinct pulsation. The chest became completely filled with fluid, and on aspiration, twenty four hours later, this fluid proved to be blood. The epigastric pulsation had now disappeared, and the pain had ceased. The man lived for five days after this attack of pain, and during this time presented very few symptoms except dyspnœa, slight fever, and marked pallor. At the autopsy

it was found that instead of being an aneurism in the lower part of the thorax it was an aneurism of the abdominal aorta. It had formed at a point opposite the cæliac axis, and had eroded considerably the first and second lumbar vertebræ, pushing its way up behind the liver, rupturing through the diaphragm. Although four litres of blood were found in the right pleural cavity the man lived for five days after the rupture.

Proceedings

of the

New York Pathological Society.

New Series, Vol. I. October and November, 1901. Nos. 5 and 6

TABLE OF CONTENTS.

Coleman and Ewing, A Case of Glanders in the Human Subject.—Schultze, A Case of Phlegmonous Gastritis.—Wood, Observations upon the Technique of Frozen Sections.—Park, Preliminary Communication of Experiments upon the Feeding and Inoculating of Calves with Human Tuberculous Material.—Herter, The Production of Coma in Monkeys from Intravenous Infusions of Beta-Oxybutyric Acid.—Schlapp, Intramedullary Degenerations of the Central Nervous System Secondary to Brain Tumor.—Dunham, A Simple Apparatus for the Anaerobic Cultivation of Bacteria.—Brooks, A Case of Miescherschen Schläuche in the Heart of an Elk.—Schultze, Post Mortem Changes in the Pancreas simulating Fat Necrosis; Adeno-Carcinoma of the Kidney.—Connor, A Case of Ruptured Abdominal Aneurysm Simulating Hæmorrhagic Pancreatitis.—Lewald, A Case of Pernicious Malarial Fever.—Lewald, Specimen of Hour-Glass Contraction of the Stomach.—Potter, A Case of Glanders in the Human Subject.

Dr. Edward K Dunham, *President.*

A CASE OF GLANDERS IN THE HUMAN SUBJECT.

warren coleman, m. d., and james ewing, m. d.

The patient, a hostler by occupation, 36 years of age, was admitted to the hospital on August 24th, 1901, complaining of a a wound in the third finger of the left hand caused three weeks before by the bite of a horse said to have had distemper. The wound had suppurated and under treatment healed about a week and a half before admission. About ten days before entering the hospital he was taken ill with headache, malaise, loss of appetite, indefinite pains in the muscles of the back and legs, and diarrhoea. The symtoms increased in severity and the patient lost flesh. There had been no chill.

On physical examination, he was found to be moderately well nourished, with flushed face and apathetic countenance, eyes suffused and dull. The pulse rate was 88 and of good character; the temperature 104.6° F. The heart was normal in size and free from murmurs, and the lungs were apparently normal. There were a few rose colored spots over the abdomen but there was no

abdominal tenderness or distention. The liver and spleen seemed normal.

The day after admission he was more apathetic and at times slightly delirious A tender and fluctuating swelling developed in the middle of the outer aspect of the left leg; the skin over it was red. The rose spots on the abdomen were more numerous and some of them were very distinctly raised above the surface. The following day, August 26th, there was active delirium and the swelling on the leg which was larger, was incised and six ounces of grayish blood-streaked pus were evacuated. It was noted that some of the rose spots had become papular and that several small papules had developed on the forehead, face, chest and back. A non-fluctuating swelling, about three inches in diameter, had appeared on the middle third of the left fore arm. The leucocyte count was 13,000.

On August 27th the swelling on the left forearm was incised and about 4 ounces of thin grayish sanious pus evacuated. Microscopical examination of this pus showed only cocci present. A few of the papules previously noted had become pustular and fresh papules had developed in the same regions. The patient from this time on began to emaciate rapidly and lost in strength. More nodular swellings had developed on the right forearm, the outer aspect of the left thigh, and on the outer aspect of the left leg about its middle third. A short hacking non-productive cough was noted at this time and the blood was tested for the Widal reaction, but the result was negative. Some of the pustules which had been ruptured by the manipulation of the nurse and attendants presented an umbilicated appearance. Subcrepitant and mucous rales were detected over both lungs. The leucocyte count was still 13,000.

On the sixth day after admission the delirium was of a low muttering character, and the eruption was more abundant.

Smears from one of the pustules showed a few cocci and fewer bacilli morphologically similar to the bacillus mallei. Cultures were taken from the pustules and 5 c. cm. of blood were removed from a vein at the bend of the elbow. The bacillus mallei was subsequently demonstrated in this blood.

The patient died on the morning of September 1st.

The autopsy was made thirty hours after death. The skin showed about one thousand papules, macules, or pustules, irregularly distributed over the body, varying in size from a pinhead to 1 cm. in diameter. They were generally acuminate, sometimes slightly umbilicated, while the largest lesions were ulcerated and excavated. Many of them resembled variolous pustules, but were more distinctly purulent and not markedly umbilicated. They were usually surrounded by a peculiar anaemic halo, 1 to 2 cm. in diameter. In some areas the lesions were confluent,

and the skin and subcutaneous tissue were indurated and discolored by hemorrhage. A few of the same pustular lesions were found in the respiratory musosa. The skeletal muscles were the seat of perhaps a score of abscesses, ½ to 3 cm. in diameter, containing thick blood-stained pus The heart was normal. Both lungs exhibited numerous consolidated areas, ¼ to ½ cm. in diameter, single or conglomerated, resembling tuberculous foci. These areas were very light colored, and were very sharply marked off from the surrounding pulmonary tissue, which was markedly hyperaemic. These nodules projected slightly on section, and on the pleural surface. They were quiet firm. The upper portion of the left lung was diffusely consolidated. The pleura was irregular coated with fibrin. The bronchial mucosa was hyperaemic, very slightly coated with mucus, and exhibited a few well-raised pustules The bronchial nodes were all hyperaemic; two of them were softened, and one of these two had ulcerated into the left bronchus, producing a large ragged ulcer of the mucosa. The pneumonic area in the left lung had resulted from the inspiration of the contents of the softened node. No other lymph nodes in the body were found to contain specific lesions. Those in the groin, axillae and along the left arm were not enlarged on palpation, and were not dissected out. The spleen was the seat of a well-marked acute hyperplastic splenitis. There was acute degeneration of the liver and kidneys The testicle and bladder were normal. The gastro-intestinal tract showed slight catarrhal inflammation, and Peyer's patches were atrophic. Over the right external occipital protuberance was a subperiosteal collection of thick, coherent pus, and between the dura and skull a similar collection. The meninges were hyperaemic and oedematous, but the brain was normal. The bone marrow in the ribs was cellular and hyperaemic. Microscopical examination of the inflamed tissues in both the human subject and in an inoculated guinea-pig showed the usual lesions of glanders. The main features of these lesions appeared to be the following: (1) An acute exudative process, the exudate being composed chiefly of leucocytes, among which the polynuclear cells were slightly in excess of the mononuclear; (2) A peculiar necrotic process affecting the exudate and the tissue involved. Karyorrhexis of nuclei and hydropic and fatty degeneration of the cell bodies appeared to be the exclusive type of necrotic process induced. The wide areas of complete coagulation necrosis seen in tuberculous foci of equally rapid formation were missing. Giant cells were not observed; (3) A striking feature, especially in the muscles, was the very sharp line of demarkation between the necrotic process and normal tissue No evidence of a productive process could be discovered.

The bacteriological study of the case consisted in the examina-

tion of smears of the exudate from various lesions, cultures from these lesions and from the blood, and the inoculation of a guinea-pig with the material. The blood which had been removed from the medium basilic vein on August 31st, was placed in two tubes of ordinary broth. These were kept on ice until Sept. 2, and were then placed in the thermostat. On September 3, there had been no growth, but on the following day an abundant flocculent growth appeared, resembling that of the streptococcus pyogenes. It was flocculent, occasionally adherent to the sides of the tube, leaving the fluid clear. Microorganisms, morphologically similar to bacillus mallei were present in pure culture. From the post-mortem blood colonies of the glanders bacillus and of various unidentified cocci developed on blood serum. Pus from the intramuscular abscesses gave the glanders bacillus and the staphylococcus pyogenes aureus. The lung yielded an abundant growth of bacillus mallei and of a large filiform bacillus. From a pustule of the skin previously penciled off with 5-per cent. formalin and sterile water, a growth was obtained of the glanders bacillus and of a large unidentified coccus. Smears of the skin lesions showed only the glanders bacilli without cocci; from the pus of the abscess, glanders bacilli and staphylococci were obtained, while from the lung only glanders bacilli developed, but in great abundance. The earliest identification of the glanders bacillus was made from a diffuse, slightly brownish growth at first in pure culture, but later overgrown by a large filiform bacillus from the lung on potato. This growth appeared in less than twenty-four hours. On September 3, a male guinea-pig was inoculated intraperitoneally with an emulsion of the lung tissue. The pig did not appear to be much affected until September 8. It died the following day. The autopsy showed a few small collections of thick pus in the skin and muscles at the site of puncture. The parietal peritoneum was granular, the visceral shiny. There was no ascites. There was one large pustule projecting prominently from the peritoneal surface of the small intestine. Peyer's patches were inflamed and swollen. The lungs and kidneys were negative. The Malpighian bodies of the spleen were prominent. The liver showed numerous small whitish foci. The testicles were much swollen, both measuring 4 cm. across. The tunica vaginalis was thickly infiltrated with the typical whitish foci of necrosis. On section, these foci were found to be limited to the tunica, and microscopically they exhibited the usual necrotic lesions of glanders. The cultures taken from the heart's blood were sterile. On broth, cultures from the testicles gave staphylococcus aureus; on blood serum the bacillus of glanders.

Discussion.

DR. COLEMAN: The abscesses were remarkably symmetrical, all of them deeply situated, and, for the most part, without signs

of inflammation in the overlying skin. The abscess cavities had no pyogenic membrane. The abscesses were intramuscular, and the pus dissected the muscles out along their sheaths for variable distances. The abscess in the lower part of the left thigh had burrowed nearly to the knee-joint. Practically no reaction had taken place in the incised wounds and the cavities remained nearly dry. Down through the incisions the muscles looked like those of a cadaver. The eruption first appeared as macules over the anterior abdominal wall, presenting much the appearance of the rose spots of typhoid. That some of them disappeared was shown by the marks placed around them with an indelible pencil, but by far the majority developed into papules and subsequently into pustules. The eruption came out slowly at first; then with great suddenness innumerable papules and pustules appeared on the forehead, face, chest and upper part of the abdomen. There were also scattered lesions on the scalp, back and extremities. During the first part of the illness the change from macule to papule and pustule proceeded slowly, occupying two or three days, but later the transition was measured by hours. The individual lesions were situated on a hyperæmic base, which, strangely enough, became anæmic after death. According to G. S. Woodhead, in Allbutt's practice, the base is anæmic sometimes during life. The nasal mucous membrane gave no evidence of involvement. The cough was due to lesions of the trachea and bronchi, as described by Dr. Ewing. None of the accessible lymph nodes were involved. From the length of the incubation period it seemed probable that the man was not infected with glanders at the time the horse bit him Woodhead states that the incubation is very short after inoculation, usually within twenty-five hours, unless the inoculation takes place through an old wound or through no apparent wound, when it may be prolonged to one or two weeks, or more. Moreover, in the former case, lymphatic involvement is prominent.

Glanders in the human subject was formerly much more frequent, the older journals containing records of many cases. The present case is the fourth, according to the records of the Health Department, that has occured in New York City since 1888, viz , one in 1888, one in 1893, one in 1899 The temperature range had been high, only once falling below 103° F., and the highest point being 105.6° F,

Dr. W. H. Park: I believe that I saw the case reported to the Health Department as having glanders in 1899. The man was between sixty and seventy years of age, in poor condition, and he had a series of small abscesses on one of his legs. These measured one to one and a half inches. Some of them had opened, and all of the abscesses were sluggish. I took the pus from two abcessess with a hypodermic needle, and scraped out two or three

others. From none of these did I obtain the glanders bacillus, and inoculations into guinea pigs proved negative. It seemed to me the case was not really one of glanders.

Dr. Lartigau: Did Dr. Ewing succeed in staining the bacilli in sections, and if so by what method. I have personally found the methods recommended rather unsatisfactory because of the rapid decolorization of the organisms.

Dr. Ewing: I have made some attemps to stain the glanders bacillus in the tissues, and have succeeded very imperfectly. With sections of intramuscular abscesses I obtained the best results. Partial success was obtained with methylene blue. Loeffler's alkaline methylene blue was not tried. Early in the summer, I was asked to examine the mucus from two or three horses on Long Island. One of the animals had died from what the Board of Health called glanders, and the other horses had contracted the disease from the first horse. The diagnosis was questioned Numerous cultures of the mucus were made on various media, but they failed to show any glanders bacilli. Then, some of the mucus scraped from the nostrils had been examined. In smears of this material a few bacilli were found, but nothing even suspicious of glanders. All the plates culture were negative. I inoculated two guinea-pigs with an emulsion of this mucus and crushed tissue. One of them died within two weeks of a slow septicaemia, and no lesions were found in the body. The other pig survived and presented no symtoms. The horses had gone on, two of them dying naturally and one being shot by the health authorities. None of them had developed farcy-buds, though the health officers and the veterinarians in the vicinity were agreed that the disease was glanders. From a conversation I was led to believe that glanders was rather common. If this be so, there should certainly be more cases in the human subject. I am of the opinion that certain cases of cutaneous and muscular pyaemia belong in this category.

Mallein was injected into the horses in several instances, and in each instance there was a rise of temperature; but for various reasons the reaction was regarded as satisfactory. The experiment of injecting small doses of mallein as a curative agent was also tried. This also yielded negative results.

A CASE OF IDIOPATHIC ACUTE DIFFUSE PHLEGMONOUS GASTRITIS.

O. H. SCHULTZE, M.D.

The specimen of stomach presented was removed from a man forty-one years of age, a native of Austria, and by occupation a

truck driver, who was admitted to the Insane Pavilion of Bellevue Hospital on June 13th, 1901. On admission his temperature was 99.4° Fahrenheit, pulse 76, respiration 22. He was very violent during much of the time; but his appetite was good until June 16th, when after partaking of food, vomiting occured This continued during the following day and he was restless, much exited, and apparently weaker. The vomitus contained bile. During that night there was evidently much abdominal pain but no tympanites. Death occurred on the morning of June 18th. The medication consisted in the administration of hyocine, atropine and morphine during the periods of active delirium, followed later by whiskey and strychnine. The lesions found at autopsy were those of sub-acute meningo encephalitis of the type usually found in cases of dementia paralytica, chronic interstitial nephritis, chronic interstitial pancreatitis, chronic perisplenitis and brown atrophy of the heart muscle. Besides this, the stomach was found markedly thickened but normal in size and form. Its peritoneal coat was smooth and glistening, and the stomach contained a small amount of bile stained mucus. Its weight was 19 oz. The mucose was bile stained and presented no solution in continuity. The stomach walls were considerably thickened and on section clear serum flowed freely from the cut surface. The wall thickness was 1 cm., the increase being chiefly in the submucosa but the muscularis was likewise thickened. The process extended into and infiltrated the first portion of the duodenum and cardiac end of the oesophagus. Microscopic study of sections by various staining methods including Weigert's showed a marked infiltration of the stroma with lymphocytes and very little atrophy of the tubules. Here and there the stroma adjoining the muscularis mucosæ showed evidences of oedema. The muscularis mucosa itself was normal, but the submucosa was the seat of marked oedema, the meshes of its fibrous tissue being distended with amorphous and granular material, which remained unstained by Weigert's method. The muscular coat was involved by infiltration of polymorphonuclear leucocytes, the infiltration seeming most marked in those portions immediately adjoining the submucosa. As the peritoneum was approached the inflammation became less and less marked. The mesothelial lining of the peritoneum was not preserved in the sections. The connective tissue layer appeared uninvolved. Sections stained for bactaria showed large numbers of short chains of streptococci most abundant in the submucosa and muscularis, none being found in the mucosa. Cultures were not made. The lesion is evidently one of idiopathic, acute, diffuse phlegmonous gastritis, since no other evidence of infection was found, nor could any evidence of injury be made out.

OBSERVATIONS UPON THE TECHNIQUE OF FROZEN SECTIONS.

F. C. WOOD, M.D.

One of the most important elements in frozen section work during operations is technique which permits rapid work in order that an early examination may made. Every minute the patient is kept under ether adds to the danger of the operation and attention should be paid, therefore, to the making of such sections as will permit of a diagnosis without regard to the finer details which slower methods permit. I have found the modified Cathcart microtome best suited to frozen section work. A simple hand bulb and ether spray are used, though it is very convenient to have a small rubber foot bulb. In warm, damp weather or in a hot operating room it is often difficult if not impossible to freeze with ether. In such cases it is advisible to facilitate the freezing of the fresh tissues by spraying them from above with ethyl chloride from one of the small glass tubes in which it is usually put up for local anaesthesia purposes. If the fragment of tissue is not over 2 mm. in thickness and both ether spray and ethyl chloride are applied at the same time, it is an easy matter to freeze such a specimen in 30 seconds. Series of sections are rapidly made and removed from the knife and dropped into a small dish of water and a suitable one selected from the number as it floats out into the water. Holding it by means of a pointed pair of forceps, the section is dipped into a small dish containing the staining fluid. I have found that a half saturated aqueous solution of thionin is the best stain for fresh tissues. It is certainly far superior to any of the other aniline dyes I have tried and it is equally good for fixed tissues. The sections are allowed to remain in the thionin for a few seconds and then removed and washed in water. The sections should never be allowed to escape from the grasp of the forceps in the process of staining or washing, but they should be shaken out of the water until all the excess of stain is removed, and then gently drawn up on the surface of the slide, covered with the cover glass and examined with a medium power lens. A drop of glycerine may be added before the cover glass is put on. As a rule this adds nothing to the clearness of the picture and it is apt to extract the stain from the preparation. The thionin stain has a distinctly nuclear selective action and preparations if thin enough will bear examination with high power. Mucoid and amyloid degenerations are differentiated by the stain. The thinness of the section will depend somewhat upon the skill of the operator and more upon the nature of the tissue. For instance, sections from a soft carcinoma of the breast or from a sarcoma may be easily obtained of the thickness of 20 microns. Hard fibrous tissues are more difficult to cut thin and

lymph nodes with their surrounding fat are also difficult to cut in thin sections. From the standpoint of rapidity, the method which I have described leaves very little to be desired. I have often cut and examined sections within two minutes or less time.

PRELIMINARY COMMUNICATION OF EXPERIMENTS UPON THE FEEDING AND INOCULATING OF CALVES WITH HUMAN TUBERCULOUS MATERIAL.

W. H. PARK, M.D.

This report is purely in the nature of a preliminary communication. The interest in such experiments has been very much enhanced by the recent communication of Koch.

Five calves weighing about one hundred and fifty pounds each were first tested with tuberculin in order to exclude existing tuberculosis. The test was negative. Four were used for feeding experiments and one reserved as a control. The calves were fed with tuberculous sputum which had been collected from tuberculous patients of St. Luke's Hospital during a period of two weeks. The sputum was in part fed with sterilized milk and in part injected subcutaneously. Two and a half months after feeding and inoculating, the calves were tested with tuberculin; three out of the four showed characteristic reactions. The autopsy of one of the calves revealed enlargement of some of the lymph nodes only. Smears from these lymph nodes showed no tubercle bacilli. Therefore, after two and a half months this calf showed no lesions of tuberculosis, except enlargement of some of the lymph nodes which contained no tubercle bacilli. The explanation for the tuberculin reaction may be found in the abcesses at the original sites of inoculation. These probably contained some living and certainly dead tubercle bacilli.

The three remaining calves have gained in weight since the inoculations.

Discussion.

DR. DOW: I should like to ask Dr. Park if the animals were subjected to inhalation experiments.

DR. PARK: The difficulties and danger of inhalation experiments did not seem to warrant their performance.

THE PRODUCTION OF COMA IN MONKEYS FROM INTRAVENOUS INFUSIONS OF BETA-OXYBUTYRIC ACID.

C. A. HERTER, M.D.

Some observers have been inclined to attribute the coma of diabetes not so much to the acid as to the presence of toxins. Klemperer of Berlin was one of those who took this view. It is, therefore, interesting to know whether the mere introduction of an acid into the circulation is capable of bringing about anything comparable to the coma of diabetes found in man. The experiments conducted with the object of testing this point can hardly be made very satisfactorily on other animals than monkeys. I used 5 per cent. acid solutions of oxybutyric acid in two experiments on monkeys. The first experiment failed through imperfect technique, but the second experiment was strikingly successful. In the first experiment, after the injection of 30 c.c. of the acid solution, the animal yawned continually and became very drowsy. After the injection of 60 c.c. the animal gave few short gasps and died. The heart-beat could not be felt during the last few minutes of life. No urine was passed during the infusion. The autopsy was entirely negative. There were 6 c.c. of urine in the bladder, and it gave a distinct reaction with ferris chloride, but ceased to give this after boiling. The urine before the injection had not given this reaction. The urine contained a small quantity of albumin. In the second experiment, after 33 c.c. had been injected, the animal rather suddenly became stuporous, and it became impossible to arouse it by pricking the skin. For two hours and a half the animal lay in a stupor, but two hours later it appeared entirely normal, and by the next day seemed as well as usual. There was complete absence of cyanosis throughout the experiment. Somewhat less than half a gram of oxybutyric acid per gram of weight of the animal was used. These experiments strengthen the view that the coma seen in the human subject is referable to the oxybutyric acid in the blood, yet I am inclined to believe that there may be contributing causes, such as infections, in some instances.

Discussion.

Dr. A. Mayer: I believe that Dr. Herter has been the first investigator to make experiments of this kind on monkeys, though similar experiments had been made on other animals, but not with the success achieved by Dr. Herter. The opinion to-day is rather prevalent that diabetic coma is produced by oxybutyric acid principally. It has been claimed that with the sugar burned up in the body other less oxidizable substances are also consumed, such as Betaoxybutyric acid (and its derivatives, diacetic acid and

acetone), and that in the healthy subject these substances do not appear in the urine. When, for some reason, as in diabetes, the sugar is not burned up, these substances appear in the urine. It has been claimed that this could be produced artificially by withdrawing the carbohydrates from healthy individuals. Apparently, to strengthen this view, Schwarz* made some observations on made some observations on the diminution of diacetic acid and acetone in diabetic subjects. These two bodies are the derivatives of the oxybutyric acid. He gave glyconic acid and sugar acid to diabetics, and marveled at the rapid diminution of the diacetic acid and the acetone in the urine in diabetic subjects. The following year† he experimented upon a case of diabetic coma under his observation. A large quantity of Beta-oxybutyric acid was found in the urine, and on a certain date, symptoms of coma had developed—dyspnœa, rapid increase of respiration and pulse, along with vomiting. The symptoms had been allowed to progress until coma developed, and then the patient was given some glyconic acid—the equivalent of 70 grams, neutralized by bicarbonate of soda. The success of this experiment was striking, as the patient in a short time came out of his comatose state and remained so for about three weeks. The patient again became comatose, and again improved under the use of the glyconic acid. A third time, two or three weeks later, coma reappeared, but the supply of glyconic acid had been exhausted, necessitating its omission. The patient died. This experiment of Schwarz seems to prove that Beta-oxybutyric acid or its derivatives are really the excitants of diabetic coma, and that perhaps we may find a substance to prevent its development, or coma having appeared, some substance which may bring the patient out of this state. Glyconic acid should be given to a monkey previous to the infusion of oxybutyric acid, and then note whether it is possible to produce coma by such an injection. I have been the first one in this country to indorse the theory of the bacterial origin of diabetes, although I did not publish my papers until 1898. Although the disease may be of bacterial origin, I am inclined to think that the coma itself is the result of the oxybutyric acid in the blood.

INTRAMEDULLARY DEGENERATIONS OF THE CENTRAL NERVOUS SYSTEM SECONDARY TO BRAIN TUMOR.

M. G. SCHLAPP, M.D.

The sections and drawings which I present show different parts of the nervous system in a case of glioma with cystic degen-

* Leo Schwarz. "Ueber Aceton-Ausscheidung.," im Congress für Innere Medicin, 1900.

†*Prager med. Wochenschrift*, Juli und August, 1901.

erations, involving almost the entire right cerebellar hemisphere. The sections are presented in order to show the secondary degen erations that take place in the nervous system in cases of brain tumor. These degenerations are not due to injury of the neuron involved directly by the growth, but indirectly by the effect which the growth has upon the whole nervous system.

Transverse sections through different parts of the spinal cord treated by the Marchi method show that the posterior columns and posterior nerve roots are alone involved. The degeneration is confined almost entirely to fibres within the spinal cord (intramedullary fibres), and the degeneration extends just to a point where the nerve fibres take their exit from the spinal cord. This fact has been pointed out by other authors (Mayer, Pick, Hoch, and others.)

Throughout the whole spinal cord, the columns of Burdack are more involved by the degeneration than the columns of Goll. Many degeneration fibres may be traced into the gray matter of the posterior horns, intermediate gray matter, and into the anterior horns of the spinal cord. The degeneration is most marked in the cervical region, less so in lumbar, and least in the dorsal region. It was found in the lemniscus throughout its course, from the nuclei of Goll and Burdack up to the thalamus. Of the cranial nerves, as in the spinal cord, the sensory ones only are involved with the exception of the oculomotorius The trigeminus nerve shows very marked degenerations, which only extend to the point of exit of the nerve from the central nervous system. The fasciculus longitudinalis posterior is also very much degenerated. The right cerebellar superior peduncle is almost entirely degenerated. This degeneration is due to the destruction of the dentate body in the right cerebellar hemisphere, which is trophic center for the right superior cerebellar peduncle. So, in this case manifestly, the degeneration is attributable directly to the destruction of the trophic center of the neuron degenerated by the tumor.

The tract of Marchi and Loewenthal in the spinal cord shows no degeneration, so that this tract has not its origin in the cerebellum, as these authors believe, but very probably has its tropic center in Deiters' nucleus, which is not injured These intermedullary degenerations in the posterior columns of the spinal cord and in the intercranial nerves are analogous to the changes in the optic nerve in brain-tumor cases.

The specimens were treated by the Marchi method and counterstained by acid rubin, which stains the nucleated sheath of Schwann a deep red. This combined staining method shows clearly that the degeneration in the posterior roots of the spinal cord, as well as in the cranial nerves, extends exactly to where the nucleated sheath of Schwann begins to cover the extra medullary nerve fibre. It is probable that the sheath of Schwann

acts in some way as a protection to the myelin substance, or myelin substance and neuraxon.

Degenerations very similar to the above are found in Addison's disease, diabetes mellitus, diphtheria, alcoholism, etc. In a crushed cord case (the cord being entirely severed in cervical region, and patient living eleven days after injury), I found degenerations in posterior roots, in lower dorsal, lumbar, and sacral regions, similar to the degenerations in the tumor case. These degenerations were intermedullary: that is, not extending beyond the point where the sheath of Schwann begins to cover the nerve fibres. They were not descending degenerations, but evidently caused indirectly by the lesion.

A SIMPLE APPARATUS FOR THE ANAEROBIC CULTIVATION OF BACTERIA.

EDWARD K. DUNHAM, M.D.

The principle upon which the apparatus presented is based is upon the well-known property of an alkaline solution of pyrogalic acid to absorb oxygen. The apparatus which I now employ allows of an anærobic condition being rapidly established, and its maintenance verified. The apparatus consists of a battery-jar in which the cultures are placed on a suitable support. Over them is placed an inverted tin can or a sheet of tin foil, and over this some absorbent gauze and an inverted battery-jar. Water is poured into the outer jar so as to form a water-seal. A mixture of pyrogallic acid and caustic potash is introduced through a bent tube passing under the edge of the inner inverted jar and opening within the apparatus above the gauze, so that the latter is kept moistened by fresh absorbent solution falling upon it drop by drop. The outer end of the tube is connected with rubber tubing to a separatory funnel placed at a higher level than the jars. The solutions of pyrogallic acid (20 per cent.) and caustic potash (30 per cent.) are mixed in the funnel under a layer of paraffin oil, to prevent oxidation of the mixture. At first the gauze is stained dark brown; when absorption is complete, a white spot appears where the absorbent solution falls upon the gauze. The rubber connection, with the separatory funnel, can then be broken, and the absorbent solution in the bent tube acts as water-seal. The oxygen is removed from the jar in about thirty minutes, and an anærobic condition can be maintained for ot least five days. The whiteness of the gauze is the guarantee that oxygen is excluded.

Discussion.

Dr. W. H. Park: In the apparatus which I use the water-seal and the gauze indicator are employed, but instead of the U-

tube a rubber cork is passed through a hole in the inverted jar, and through this two glass tubes, tipped with rubber tubing carrying pinch-cocks, are passed. The pyrogallic acid solution drops directly through one cock upon the gauze. I usually make use of hydrogen for the purpose of displacing the greater part of the oxygen in the apparatus, and the pyrogallic-acid solution only to remove the final portions of oxygen. The tubes passed through the rubber cork allow this to be done with the Dunham apparatus. The drop of pyrogallic acid solution adhering to the tube outlet suffices to make an indicator almost as good as the gauze.

Dr. Dunham: Anærobic bacteria, *e. g.* tetanus bacillus or the bacillus aerogenes capsulatus, grow perfectly well in the top of a pile of Petri dishes, covered over completely with tin-foil, within the apparatus described. The foil acts as a metal bell, and it appears that the diffusion of gases is sufficient to remove all but, perhaps, the smallest possible trace of oxygen.

A CASE OF MIESCHERSCHEN SCHLÄUCHE IN THE HEART OF AN ELK.

HARLOW BROOKS, M.D.

This form of infection might easily be mistaken for trichinosis. The specimen was taken from an elk belonging to the New York Zoological Society. It had been sick for a long time. Beneath the endocardium, and all through the muscles, were to be seen small white foci closely resembling those of trichinosis. In this specimen they are not calcified, but they are frequently so. Examination showed the presence of the Miescherschen Schläuche. This parasite is a member of the sarcosporidia and has been found a half-dozen times in the human subject, but not in this country or in England. Its presence in the laryngeal muscles has been reported. The parasite is a falciform body, and is usually found within the muscle fibre where it poliferates. The spore itself is curved and has a double contour. The chromatin is usually arranged in two distinct masses, but the whole parasite will take a sufficiently active chromatic stain. It reacts to the Gram stain. It varies in size from one-third to twice the length of the hay bacillus. Its presence in the tissues gives rise to very little local reaction, differing in this respect greatly from trichinæ. A deposition of lime salts eventually results thus giving rise to granules very closely resembling the masses found in cases of trichinosis. The parasite is much more distinctly seen in fresh than in hardened or stained specimens.

Discussion.

Dr. Miller: The specimen is interesting to veterinarians, because it is so widespread among the lower animals. This particular case was interesting from the fact that the disease had proved fatal. German authorities claim that very few sheep are found in the slaughter-houses of Germany without these parasites in the diaphragm, and it is even more common in the swine of that country. It is not always easy to differentiate it from the trichina. As a rule, the muscle fibre up to the parasite itself is free, while in trichinæ back from the poles in each direction, there is always a line of demarkation of broken-down muscle. By applying a weak solution of acetic acid, one can, as a rule, bring out a membrane, which is not the case with calcified trichinæ. Experiments on feeding healthy animals with the meat of other animals containing these parasites have given negative results, and if it is transmissible there should be a vast number of such cases. The muscle is obliterated by pressure, but the parasite does not invade the muscle. The heart of this elk was flabby and very pale.

POST-MORTEM CHANGES IN THE PANCREAS SIMULATING FAT NECROSIS; ADENO-CARCINOMA OF THE KIDNEY.

O. H. SCHULTZE, M.D.

The pancreas which I present was taken from a male, thirty-eight years of age. The man was found dead in the toilet. He was very obese, and the cause of death was found to be a laceration of the omentum. The abdominal cavity was filled with blood. There was an enormous direct inguinal hernia, which was filled with both fluid and clotted blood. At the internal ring, immediately beneath the peritoneal coat, was considerable ecchymosis. The hernia had contained a large amount of reducible omentum, and in the effort of straining at stool the mass of omentum passing into the sac was torn, and the hemorrhage thus produced. The pancreas in this individual was the seat of a very large amount of fatty change. The pancreas being fresh, it occurred to me to place the organ directly in cold storage. After twenty-four or forty-eight hours under such circumstances a grayish color would appear wherever there was fat. The areas of pancreas in the fresh specimen had been pink; after twenty-four hours these areas were of a distinctly grayish-white color. This tissue, when examined under the microscope, exhibited all the

appearances of fat necrosis. The differentiation from post-mortem fat necrosis may be easily made by the coincident occurrence of pancreatic digestion of the cells. In addition to fat necrosis, there is in this specimen cirrhosis of the pancreas.

The other specimen presented is a kidney which was removed from a woman twenty-nine years of age. Almost all of the parenchyma was occupied by a tumor, which presented on section a number of lobules. Here and there, between these lobules some kidney tissue could be seen. Microscopical examination showed the tumor to be of the alveolar type of carcinoma. This kidney presented practically the same appearance as some cases of carcinoma of the pancreas, namely, an almost insensible change from normal to carcinomatous tissue. Here and there, the kidney was infiltrated with polynuclear leucocytes. The sections also show fuchsin bodies, varying in size from one-fourth the size of a blood cell to ten times that size. Some of them present no nucleus whatever. These bodies are probably the result of a peculiar change in the epithelial cells themselves, and are not formed by inclusion.

A CASE OF RUPTURED ABDOMINAL ANEURYSM SIMULATING HAEMORRHAGIC PANCREATITIS.

L. A. CONNER, M.D.

This is a specimen of ruptured abdominal aneurysm which taken in connection with Dr. Schultze's specimen, is of considerable interest. It simulated clinically hemorrhagic pancreatitis. The specimen was taken from a male Japanese, thirty-eight years of age, a steward on one of the warships in the harbor. According to the history, the man had been in good health, and while on shore-leave had been suddenly seized in the middle of the night with intense abdominal pain. He had been brought to the hospital within an hour or two, and on admission there had been excruciating paroxysmal pain referred to the left hypogastrium. When I saw him a few hours later, the man was having attacks of intense pain, with periods of remission. There was constant retching, although very little vomiting. The pulse was rapid and feeble and indicated marked shock. The abdomen was distended and tympanitic, moderately tender and very rigid all over the left side. There was good diaphragmatic breathing. The temperature was 90° F., and the pulse 124. The leucocyte count was 21,000, curiously enough. The case was a puzzling one, and in making the diagnosis hemorrhagic pancreatitis was thought probable. In the left flank, one could make out indistinctly a mass like a greatly enlarged spleen. The patient's appearance had not been that of

a man who was bleeding profusely, but later in the day he became markedly anæmic, died about fourteen hours after the attack. Although there was no syphilitic history, there was a well-marked scar on the penis. At the autopsy the peritoneum contained a little blood-stained fluid, and behind the peritoneum, and pushing all the viscera forward, was an enormous mass of blood, chiefly on the left side, extending down to the margin of the pelvis and infiltrating the mesentery, the mesocolon, and the mesentery of the spleen, and entirely surrounding both kidneys. The pancreas lay in the mass. On removing the aorta, an aneurysm was found presenting just above and to the right of the pancreas. The aorta was the seat of extensive atheromatous degeneration, and the degeneration was extreme near the diaphragm.

A CASE OF PERNICIOUS MALARIAL FEVER.

I. T. LEWALD, M.D.

The organs presented were removed from a man, twenty-three years of age, who was admitted to Bellevue Hospital on October 19th, 1901. He gave a history of having been ill for about two weeks with prostration and moderate diarrhoea on admission. The temperature was 98 4° F., pulse, 100, respiration, 70; the temperature shortly after admission rose to 104°. Physical examination revealed slight enlargement of the spleen. The diagnosis made at first was that of typhoid fever, but the blood tested for the Widal reaction gave a negative result. The blood was also examined for plasmodia, but these were not found. Five days after admission numerous aestivo-autumnal parasites were found. In a general way it was calculated that about 5% of the red blood cells obtained were infected. No crescents were found. The patient was then given large doses of quinine but died on the following day. The autopsy examination showed extreme congestion of the brain with punctate hemorrhage in the pons and cerebellum. Microscopical examination of these portions of the brain showed extreme congestion but failed to reveal any extravasations of blood. There was parenchymatous degeneration of the heart muscle, liver and kidneys. The liver further showed pigmentation, and the kidneys some chronic diffuse nephritis. A large number of malarial parasites were demonstrated in the capillaries of the kidney. The spleen lesions were those ordinarily met with in cases of fatal malaria. The pancreas was congested and somewhat enlarged. The stomach presented a small ulcer on the posterior wall and the intestine showed marked mucous membrane congestion. The pia mater of the spinal cord was congested. The retroperitoneal lymph nodes were soft and swollen.

Discussion.

DR. EWING: Were any malerial parasites found in the urine?

DR. LEWALD: The hospital record does not state whether pigment or parasites were found in the urine. It is probable that no examination was made with this object in view.

SPECIMEN OF HOUR-GLASS CONTRACTION OF THE STOMACH.

L. T. LEWALD, M.D.

The specimen which I have the pleasure to present was taken from a woman, sixty years of age, who died from the results of longitudinal and lateral sinus thrombosis of the brain and embolism of the pulmonary artery.

The point of contraction in this specimen is at the junction of the middle and distal thirds of the organ. The lumen at the point of contraction is just sufficient to admit the index finger. Since there were a number of adhesions between this part of the stomach and the surrounding viscera it is assumed that the contraction followed an old ulcer in this locality.

A CASE OF GLANDERS IN THE HUMAN SUBJECT.

N. B. POTTER, M.D.

This case was observed while an interne of the Massachusetts General Hospital, upon Dr. F. C. Shattuck's service. The patient was a male, thirty years of age, who entered the outdoor department with a story of having had pleurisy in the left side for four days. There had been some pain in the abdomen, and he had been feverish and chilly, but had had no distinct chill. There was nothing else of importance in the history except that he was a hostler. Physical examination showed a large, soft spleen, and a few fine moist râles at the end of the inspiration at the base of the left lung, and in the left axilla. The patient had an irregular septic temperature. At first, he was thought to be suffering from a rheumatic pleurisy. After having been in the hospital for about four days, a red spot developed at the bend of the left elbow, but did not go on to suppuration. Other spots formed on the lower extremity, and these suppurated. One of these was opened and the pus examined, but no organism found. After he had been in the hospital for three weeks, a culture was made from the median vein, but it proved negative. The blood failed to give any Widal reaction, and the blood examination was negative, except for the

presence of a polynuclear leucocytosis, which increased as the disease progressed. The foci of inflammation spread and became more numerous. The man was then transferred to the surgical side, and several abcesses operated upon. Although some of the abscesses appeared small, on incising them it was found that the pus had burrowed very deeply. No bacilli were found, but some of the pus was injected into the peritoneum of a guinea-pig, and the animal promptly developed a characteristic swelling of the testicle. The man died about five weeks after admission. There was a purulent infiltration of the right forearm near the elbow, near the left ankle joint, on the second toe of one foot, together with an osteomyelitis and numerous pustules in other situations, a purulent synovitis of the right knee-joint, glanders of the nasal mucosa and of the epiglottis, also a chronic pachymeningitis, together with acute degeneration of the liver and spleen.

Proceedings

of the

New York Pathological Society.

New Series, Vol. I. December, 1901, and January, 1902. Nos. 7 and 8

TABLE OF CONTENTS.

Herter. Observations on the Iso-Agglutinating Action of Human Serum.—Biggs, A Case of Phlegmonous Gastritis.—Thayer, Study of a Case of Dermatitis Exfoliativa.—Thayer, Billiary and Pancreatic Stasis due to Atresia of the Papilla.—Biggs, Syphilitic Stenosis of Bronchi.—Dow, Dissecting Aneurysm of the Arch of the Aorta.—Wilson, A new Animal Holder. Lewald, A Case of Thrombosis of the Pulmonary Artery.—Thayer, Specimen showing Result of Gastro-enterostomy for Carcinoma of the Pylorus.—Bolduan, Report of a Case of Pernicious Malarial Fever.—Wightman, The Value of the Eosinophile Count in the Differential Diagnosis of Blood.—Brooks, A Case of Cutaneous Pigmentation with Lesions in the Adrenal Glands.—Larkin, Primary Pigmented Sarcoma of the Fourth Ventricle of the Brain.—Libman, Mesenteric Abscesses with Secondary Thrombosis of the Mesenteric and Portal Veins.—Wood, Dermoid Cyst of the Ovary with Carcinomatous Changes.—Lewald, Multilocular Echinococcus Cysts of the Liver.

Dr. Edward K. Dunham, *President.*

OBSERVATIONS OF THE ISO-AGGLUTINATING ACTION OF HUMAN SERUM.

C. A. HERTER, M.D.

This paper is essentially a preliminary communication. Iso-agglutination may be defined as the close clumping or agglutination of human red blood cells by serum from another human being. The test may be made as follows: 2 c.c. of the serum to be tested are mixed with 1 c.c. of red cells separated by means of the centrifuge. When the serum of a normal or a pathological individual is mixed with the cells of the same individual in the proportion named or in other proportions the cells show no peculiarities, but lie in rouleaux or as separated individual cells. When the phenomenon of iso agglutination takes place the serum is brought in contact with cells of another human individual. The reaction may be noticed in from 2 to 5 minutes. The serum and cells after being well stirred in a watch glass with a glass rod soon show evidence of the beginning of the characteristic reaction,

when the mixture runs from side to side. Instead of appearing homogeneous the mixture shows many light spots in which there is serum but no cells. These spots increase in number and size, and it is soon evident that the cells are becoming separated from the serum in the form of a comparatively close meshed net-work. The red cells are found closely packed together in large masses and no longer have the rouleaux distribution. They have undergone a change in consistence rendering them more plastic than normal, as shown by the distortion resulting from pressure of the cover glass. The reaction may be observed with the unaided eye when the test is made on a watch glass or cover glass.

This gross phenomenon is new to me and thus far I have been unable to find any description of it. The reaction was obtained in nearly one-third of all the cases in which the blood was subjected to this test. Most of these patients were alcoholic.

It was found possible to expose the serum to a temperature of 56° F. for one hour without affecting the reaction in the least. In two instances I exposed the serum to a temperature of 50° F., in one case for half an hour and in the other for an hour. The only effect of this seemed to be a diminution in the intensity of the reaction which followed.

Ordinarily, human serum is capable of agglutinating normally the red blood cells of the dog and rabbit. No relation between this reaction and the haemolytic action of serum was observed. It has not yet been determined whether or not an intermediary body is necessary for the development of this reaction. As to the clinical significance of the phenomenon I am unable to say very much, but this field of research seems promising and fertile.

Discussion.

Dr. Janeway: Does the serum from these cases agglutinate the red blood cells of other patients, giving the reaction with normal red blood cells, and does the serum from a normal person not giving the reaction agglutinate the cells from these patients, —in other words, is there a mutual reaction ?

Dr. Herter: This condition does occur.

Dr. Ewing: The contribution of Dr. Herter reminds me of certain remarks made by Dr. Richardson of Boston at the last meeting of the American Association of Pathologists and Bacteriologists on the interaction of specimens of human blood on one another and on the typhoid bacillus. Dr. Richardson found that in some cases of typhoid fever not giving the Widal reaction, the addition of normal blood to that of the patients' induced this reaction at once. He further found that when typhoid bacillus and normal serum were mixed in a certain order the blood reaction was also obtained; but that this reaction did not occur at all when the specified order of mixing was not observed. The subject is

entirely new to me and seems to deserve further consideration. The morphology of the red blood cells would be of extreme interest to me under these conditions. It seems possible that the envelope of the red blood cells play an important part in the phenomenon.

A CASE OF PHLEGMONOUS GASTRITIS.

GEORGE P. BIGGS, M.D.

The specimens which I present are those from a case of phlegmonous gastritis admitted to the New York Hospital with the following history:

C. E., forty years of age, German, female, and by occupation a tailoress. Previous history was one of exceptional good health. Menstruation ceased five months ago, but for the past three weeks the patient has been flowing most of the time. No history pointing to an abortion.

She was taken sick eight days before admission and has been in bed ever since The chief symtom was vomiting, which, however, was not very frequent the last few days before admission. The sickness began with a chill, followed by fever and pains all over the body, which later became limited to the epigastric region. From a physician who saw her twice prior to admission it was learned that her temperature had been 100° F., respirations 30 and pulse 90; that she was slightly jaundiced, vomited frequently, and that her bowels were loose. Abdominal pain had been cramp-like and intermittent.

The following notes were made at time of entrance into the hospital: Anxious expression; respirations rapid; thighs flexed; tongue dry, coated and fissured; breath fetid; abdomen markedly distended and tympanitic; tenderness in epigastric, umbilical and right hypochondriac regions; temperature, 100⅘° F.; respirations, 44; pulse, 144; urine, 1013, acid, reddish yellow, turbid, fair amount of albumen, no sugar, uric acid, crystals, granular casts. High enemata ineffectual. Condition too critical to warrant operation. She died the following morning, temperature in the meantime having risen to 102⅘°.

Autopsy.—Body well nourished. Rigor mortis marked. Abdomen distended and tense. Peritoneal cavity contained 1000 c.c. of moderately thick yellow pus without distinct fibrinous element. The pus was very generally distributed, though rather more abundant in the upper portion of the abdominal cavity. There was no offensive odor to the pus and no gas was present. The stomach measured 25 x 11 cm., and contained a small amount of bile-stained fluid. It was of yellowish color, covered with pus,

and showed a few distinct foci of pus 1 to 2 mm. in diameter just beneath the peritoneum. Purulent infiltration had caused great thickening of the wall everywhere, except in a narrow strip 4 cm. in width, along the greater curvature in its cardiac two-fifths.

In the infiltrated parts the wall measured ¾ to 1¼ cm. in thickness, the greatest thickening being in the pyloric portion, where the submucous coat alone was ¾ cm. in thickness. The mucous membrane was slightly thickened, congested, and in many parts hemorrhagic. Over the anterior wall of the pylorous it was completely destroyed over an area measuring 1 by 1½ cm., the base of the ulcer being formed by infiltrated submucosa. A larger ulcer, also in the anterior wall of the stomach, about 2½ cm. from the pylorus, was of similar appearance, but irregular in outline. Its main part measured 3 cm. vertically and ¾ cm. transversely, and a branch extending from it toward the pylorus measured ¾ x ½ cm. The mucous membrane near the ulcers and forming borders was quite thin, suggesting that the ulceration was secondary to the purulent infiltration of the submucosa. The pus from the peritoneal cavity contained myriads of streptococci, and the same organisms were obtained in pure growth from it.

Spleen was twice its normal size, congested and soft.

Kidneys showed a moderate degree of acute diffuse nephritis, and slight chronic interstitial nephritis. Lungs were much congested and œdematous. Uterus was moderately enlarged, wall thick and firm, endometrium roughened, and cavity contained a small amount of clotted blood. All other organs were normal except for parenchymatous changes incidental to any infectious process. So far as could be determined the infection of the stomach was primary.

A STUDY OF A CASE OF DERMATITIS EXFOLIATIVA.

A. E. THAYER, M.D.

No clinical history was obtained from this case. The patient was a woman of thirty who had chronic tuberculosis of both lungs, associated with dermatitis exfoliativa. At the autopsy there were some scattered submucous hemorrhages in the stomach. The colon showed tubercular ulcers, and the mesenteric nodes were enlarged and caseous. There was also atresia of the vagina. On microscopical examination, the kidney showed some chronic parenchymatous degeneration without much interstitial change. The spleen showed marked interstitial increase and proliferation of the endothelia in the small vessels. The liver showed fatty infiltration of the peripheries of the acini and young connective tissue about the vessels. The mucosa of the stomach was œde-

matous and the outer epithelia degenerated. In the mesenteric nodes many giant cells were found. The lungs were the seat of chronic tubercular and recent lobar pneumonia. In the adrenals the nuclei of the cortex showed hyperchromatosis, and the epithelia of the medulla were deeply pigmented. There was a well marked corneous desquamation of the upper layers of the skin. The supra-papillary layers were very thin in some places and absent in others. The lymph spaces were dilated and there was a proliferation of the epithelia in the sweat-glands. There was a recent round-cell infiltration about the cutaneous blood vessels. In the outer portion of nearly every papilla there were from one to half a dozen large curomatophores containing yellow-brown pigment in coarse granules. The sciatic nerve and the breasts were the seat of fibrous hyperplasia. In other words, there was connective-tissue increase in kidneys, spleen, liver, lungs, breast, sciatic nerve and skin. This skin lesion might be a part of the general fibrosis, the result of the circulation in the blood of the toxins of tuberculosis. The coincidence of dermatitis exfoliativa and tuberculosis of the viscera had been noted in many cases.

BILIARY AND PANCREATIC STASIS DUE TO ATRESIA OF THE PAPILLA.

A. E. THAYER, M.D.

The patient from whom these specimens were removed was a man who for several years had been ill; the chief symtoms being progressive loss of strength and vomiting of blood. At that time he had been treated at Bellevue by some surgical procedure, the nature of which could not be determined. He had lived in apparent health for three or four years and then reentered the hospital three months ago with jaundice. He was emaciating rapidly. The stools were typically acholic. There was a temperature of from 100° to 101° F. in the afternoon, with occasional higher degrees. The blood count showed a leucocytosis of 18,000. Under the free border of the ribs was a large, fluctuating gall-bladder. This was aspirated and about one pint of thin, clear fluid withdrawn. A suspicion of malignant disease of the liver or bile-ducts arose, and an exploratory incision was made; but the patient died shortly afterward. The anterior thin margin of the liver showed some recent extravasation of blood and lymph. The liver showed a marked increase of fibrous tissue confined almost wholly to the distribution of the biliary passages. There was, however, no disseminated cirrhosis. The common bile-duct and its main branches, and the pancreatic

duct were enormously dilated, and the cystic duct was moderately dilated. On gross examination there was also a well-marked interstitial pancreatitis and interstitial fibrosis in the heart and kidneys. Microscopically the pancreas showed marked dilation of its ducts, some bile staining, and a very well developed interstitial pancreatitis with atrophy of the parenchyma, the islands of Langerhans having been almost entirely spared. In the middle portions of some hepatic acini there were deeply pigmented cells. Many of the small biliary radicles were plugged with polynuclear leucocytes, a fact which agreed with the clinical symtoms of fever and leucocytosis. The papilla of the duodenum had been converted into a tough mass without any lumen. The gall-bladder was found at autopsy filled with a recent clot, probably the result of the puncture of the aspirating needle. The case is of interest because of its bearing on the etiology of biliary cirrhosis. If biliary cirrhosis (Charcot-Hanot) arises from irritants conveyed through the biliary passages, why was it not present in this case? A most marked proliferation occurred about the bile passages, but in the tissue between there was no "unilobular" or "unicellular" cirrhoris. Another aspect of the case is the bile staining in some of the pancreatic cells adjacent to the dilated ducts, which is of interest in relation to interstitial pancreatitis. Experimental injection of bile into the duct of Wirsung is followed by this lesion in animals. There was no evidence of duodenal ulcer or of duodenal hemorrhage.

Discussion.

Dr. Herter: Dr. Draper and myself saw this patient. According to my recollection, the man stated that he had not been jaundiced at the first attack. He suffered from gastric symptoms which had finally culminated in hemorrhages from the stomach. These had been the only striking features about the case, clinically. The patient stated that after an operation done at Bellevue Hospital he had been greatly relieved and had gained in weight and strength rapidly, and the pain had ceased. He remained well until three months before admission into the hospital, when he complained of sharp lancinating pains in the right hypochondriac region. Jaundice soon followed. During the last month of of his illness, jaundice had become extreme. It had been very difficult to say whether or not there was any relation between the first attack and the final illness, but my feeling had been that it could hardly be a malignant disease owing to the length of time that the man had been ill. There was a history of syphilitic infection eight years before. Gall-stones had been suspected and an operation had been done for the relief of this condition. The case seemed to me one of unusual interest because the changes in the liver and pancreas seemed to point to an atresic condition of

the papilla. I regret that no examinations were made for sugar in the urine, inasmuch as pancreatic injuries are often associated with glycosuria. Where slight jaundice and slight temporary glycosuria are present, injury to the pancreas may be suspected.

Dr. Janeway: During the last few years I have seen several cases bearing on this point. In one case of catarrhal jaundice, after four years, sugar had appeared and had persisted until sugar had been eliminated from the diet. Since the disappearance of the jaundice, the glycosuria has not returned irrespective of the diet observed. Another case, that of a man who had been troubled with gall stones, ten years previously, and who had more recently had frequent chills, fever and sweating, with emaciation, and in which the examination of the blood failed to show the plasmodia or leucocytosis, sugar was found in the urine to the amount of 4½%. In two months, the sugar disappeared except after errors in diet and the jaundice and fever also disappeared. These cases are very suggestive of subinfection of the pancreas associated with stoppage of the outflow of bile. The case reported by Dr. Thayer suggests to me the possibility of their having been a duodenal ulcer, with profuse hemorrhage at the time of the man's earlier illness.

SYPHILITIC STENOSIS OF BRONCHI.

GEORGE BIGGS, M.D.

The specimen presented is of great interest from two standpoints. First, from the degree of thickness of the bronchi; and 2nd, from the etiology of the lesion. The organs were taken from a woman, thirty-five years of age, who, according to the clinical history, had been well up to the night preceding her admission to the hospital. At that time, she was seized with what was said to have been an attack of asthma. When admitted to the hospital, the dyspnoea was of a peculiar type, being entirely inspiratory and suggesting laryngeal stenosis. The larynx was normal, and it was assumed that the dyspnoea was due to the pressure of a thoracic aneurysm. Because of the high temperature, pneumonia was suspected; but the physical examination was inconclusive. The patient died the following day.

At autopsy the trachea was found thickened and slightly flattened laterally. The bronchi generally on the right side were thickened to a marked degree, and there was such stenosis of the main branch going to the lower lobe that it would admit a probe only 2½ mm. in diameter in its first centimeter. Beyond this region it was dilated again to a diameter of 1 cm. The left primary bronchus also was thickened and in its first centimeter was so stenosed as to admit a probe only 1½ mm. in diameter. The

balance of this primary bronchus was dilated to a diameter of 1½ cm. The smaller bronchi of the left side were not materially altered. These marked stenoses explained the dyspnoea and the absence of the usual signs of consolidation. There was lobar pneumonia of the whole right middle lobe, the anterior half of the left lower lobe and a small portion of the left upper lobe. The liver was moderately enlarged and contained much amyloid material. Though not greatly enlarged, the spleen presented the typical "sago" type of amyloid deposit. There was marked chronic diffuse nephritis, but no distinct amyloid reaction was obtained. The aorta showed extreme chronic arteritis with slight calcification.

In addition to the peculiar appearances of the lesion itself, the syphilitic character of the bronchial stenosis was thought to be clearly demonstrated by the amyloid deposits and chronic arteritis.

Discussion.

DR. JANEWAY: I should like to ask Dr. Biggs if there was a large accumulation of secretion behind point of the stenosis. I have seen such a condition in connection with dilatation of the bronchi.

DR. BIGGS: There was no accumulation of secretion back of the stenosis.

DR. EWING: It seems to me that the dilatation back of the point of obstruction may be explained on a mechanical basis. As the air gradually made its way through this constriction the pressure under which it entered the cavity would be limited by the suction force of inspiration. In reality, the pressure of the air on the bronchus during expiration would be greater than during inspiration and thus might lead to a dilatation of the bronchus beyond the point of the constriction. The blocking of the constriction by mucus would tend still further to increase the pressure by obstructing the outflow of air.

DISSECTING ANEURYSM OF THE ARCH OF THE AORTA.

E. L. DOW, M.D.

The specimen presented this evening is one illustrating the extreme lesion of acute dissecting aneurysm of the thoracic aorta, presumably induced by severe muscular exertion. The case was that of a man of forty, who had previously felt perfectly well.

He denied syphilis and alcoholism and the previous occurence of attacks of dyspnoea. He said that while subjecting himself to a severe strain in repairing an engine, he suddenly felt that he was losing consciousness, but experienced no pain, and afterward remembered no other accompanying sensation. He fell to the floor. The ambulance surgeon found the man unconscious and suffering from extreme dyspnoea. The heart's action was irregular and rapid, and there was a long, loud, medium-pitched blowing systolic murmur heard over the entire præcordium Its maximum intensity was at the apex, and it was transmitted to the left. The right radial pulse was much smaller than the left. On reaching the hospital the pulse was imperceptible, and the skin cold and clammy; the heart's action was extremely irregular; the lungs were filled with the rales of pulmonary œdema. He rallied somewhat under the use of oxygen inhalations and stimulants, and in six hours had sufficiently recovered to give the foregoing history. He rested comfortably through the day, but in the evening complained of inability to use his right arm. Early the next morning, or thirty hours after the onset of the illness, he was suddenly seized with severe dyspnoea, and became unconscious. Examination showed an acutely dilated heart and marked pulmonary œdema. He died in a few minutes.

The autopsy was performed eight hours after death. Between the aorta and the pulmonary artery an extravasation of blood could be seen. The heart muscle was flabby, and the cavities moderately dilated and filled with a large amount of post-mortem clot, and a small amount of white blood clot. The mitral orifice admitted the tips of five fingers, and its cusps were normal. The aortic orifice was large, but its cusps approximated perfectly. A rent was discovered in the floor of the aorta about four inches from the aortic valve. This rent was transverse, measured three-quarters of an inch in length, and was situated in the floor of a small patch of fatty degeneration of the intima and media, through which it extended. The adventita was not involved. From this rupture of the coats of the aorta had been dissected up to within half an inch of the aorta valves. The aneurysm completely encircled the aorta for a distance of one and one half inches near the heart, and also extended up the inner half of the right common carotid for an undetermined distance, and completely encircled the innominate and left subclavian. At one and one-half inches from the aortic valve was another completely encircling transverse tear of the inner aortic coats. The cavity produced by the dissection contained about three ounces of dark blood clot. In other respects the aorta was normal except for a few patches of fatty degeneration of the intima. The liver, spleen and kidney showed nothing but acute congestion. The adrenals were unusually fatty. The stomach and intestines were filled with gas, and the contents of the ileum and colon were soft and green.

The brain and its coverings were apparently normal. There was no atheroma of the cerebral arteries, and no thrombosis or embolism could be made out. There was no evidence of syphilis.

A NEW ANIMAL HOLDER.

ROBERT J. WILSON, M.D.

The animal holder demonstrated has been used by me for the last five years. It has the great advantage that it may be used without the aid of an assistant, and the ease with which one may be constructed strongly recommends it to laboratory workers.

It consists of a box with a sliding lid; the lid having a slit in the anterior end that engages the head of the animal, and on its under side a dam, which represents the posterior wall of the box and prevents the animal from backing out. The lid has on its posterior end two small slits just large enough to accommodate single links of small dog chains, which are used for holding the animal's legs in abdominal operations.

For operations about the head, or ear-vein inoculations the lid having been previously removed, the animal is placed in the box, the lid is slipped in, the slit in its forward end catching the animal's neck while at the same time the buttock dam on the under side of the lid pushes the animal's chest up against the anterior wall of the box, where it is held firmly and practically immovable in place without being tied in any way or made to suffer by restricting strings.

In securing the animal for abominal operations, it is allowed to stand on the table or floor, the lid of the box is held above its neck with the buttock dam pointing in the same direction as the animal's head. The lid is then lowered so that the slit in its anterior end embraces the animal's neck. The animal is then grasped firmly by its hind legs and drawn up so that it lies with its back on the board, with its hind legs completely extended.

These are secured in its place by two small dog chains which are fastened about the legs just above the knees by slipping loops, and secured to the lid by having the links of the chains held in the slits at the posterior end of the lid provided for that purpose. The lid is then slipped into place with the animal's head in the box, and body lying exposed on the top. The small dog chains are particularly desirable, because they do not constrict and hurt the animals and do not require knots of any kind.

The following dimensions are for rabbits of 1500 grams weight, but the holder can be made suitable for almost any sized animal.

Box.—Inside dimensions, length 14½ inches, heights of side walls, 4½ in.; height of front wall, 3¼ in. The front wall is also 2 in. thick. The posterior wall is represented by the buttock dam on the lid. Dimensions of Lid.—Length 28 in., width 4 in., thickness ½ in. Slit in anterior end of lid is 4¼ in. long, 1½ in. wide at its anterior end, and ¾ in. wide at its posterior end. The buttock dam is fastened to the under side of the lid 10½ in. from its anterior end, and is 3½ in. long, 2¾ in. wide, and ¾ in. thick. The dog chain links should not be more than ⅜ in. long, and of the open-link variety.

SPECIMEN SHOWING RESULT OF A GASTRO-ENTEROSTOMY FOR CARCINOMA OF THE PYLORUS

A. E. THAYER, M.D.

The operation of gastro-enterostomy in this case was performed one year ago with the aid of a Murphy button. Since then the man been able to eat freely and had done well, dying from other causes than those attributable to the operation. At the post-mortem, the pylorus was found absolutely without lumen While just back of it was the artificial opening formed at the operation leading into the jejunum about half a meter from its upper end.

A CASE OF THROMBOSIS OF THE PULMONARY ARTERY.

L. T. LEWALD, M.D.

The specimen exhibited presents the usual lesions of thrombosis of the pulmonary artery. This artery, as well as the aorta, showed well-marked patches of endarteritis. The thrombosis was a large one and formed in a branch leading to the lower lobe, thus shutting off the blood supply to nearly all of this lobe. At the time of the autopsy this lobe was the seat of extensive hemorrhagic infarctions. There was also a thrombus in the left ventricle of the heart. The case is interesting because of the occurrence of thrombosis in the two blood systems.

Discussion.

Dr. Coleman: Was there any evidence of the dilatation of the right heart in this case?

Dr. Lewald: The right heart showed no marked dilatation, but there were some hypertrophy of the wall of the right ventricle and moderate stenosis of the mitral valve.

REPORT OF A CASE OF PERNICIOUS MALARIAL FEVER.

CHARLES BOLDUAN, M.D.

The slides presented from these case of pernicious malarial fever contain a considerable number of æstivo-autumnal parasites. The interest in the case is chiefly from the standpoint of its fatal issue. The first case was of the algid type, and the other of the comatose variety. The first patient was twenty-two years of age, had come from Cuba and had not been ill previously. Five days before coming under my observation he had felt dizzy, he had muscular pains, and had vomited some black material. There had been no chills and the bowels were regular. Physical examination showed no enlargement of the spleen and no typhoid eruption. The temperature followed the regular quotidian type, but there were no chills. Examination of the blood showed a large number of signet rings On the fourth day the patient felt exceedingly well and desired to go home. A few hours later his pulse suddenly became weak, and he died the same evening.

The other case was that of a Spanish fireman on a ship. He was admitted to the hospital with a temperature of 105° F Eight days previously he had been taken ill with fever and chill, and on the day of admission had been found in his bunk unconscious The blood count gave 19,000 leucocytes, and the Widal and diazo reactions were negative. There was some albuminuria. Examination before the blood showed severe infection with malaria. Quinine was given hyperdermically but he died on the third day.

No autopsy was permitted. As the leucocyte count was taken immediately after an ice bath, it is probable that this explains the high count.

THE VALUE OF THE DIFFERENTIAL COUNT IN THE DIAGNOSIS OF BLOOD.

O. S. WIGHTMAN, M.D.

This paper is based on the results of the study of blood smears from different animals The smears were stained with Ehrlich's tri-acid stain. The counts were based on a study of five hundred cells in every instance, and included blood from the sheep, pigeon, gray rabbit, calf and goat. From the investigations of a number of workers it seems probable that the origin of the eosinophilic cells is in the bone marrow. It will be remembered that a normal percentage of these cells in the human blood varies from one-quarter of one per cent to four per cent. Under patho-

logical conditions the eosinophile count may be greatly increased from various causes. An analysis of the different tables of my results in animals shows that there normally exists a rather high lymphocytosis varying from a minimum of 34% in the goat to a maximum of 97.6% in the pigeons. Moreover, the animals quite regularly showed a rather low polymorphonuclear count.

Discussion.

Dr. Wood: I have been especially interested in tracing a possible connection in a large number of eosinophiles in the blood and the presence of tape worms in the intestine. I have studied cases containing both the round worm and tape worms, but found no increase in the eosinophiles though such an increase has been observed in a large number of cases Quite recently I saw a case in which a considerable increase in the number of eosinophiles in the blood was observed which led me to suspect tape worms although no segments of the worms had been found. Subsequent examination, however, revealed them. The percentage of eosinophilic cells at this time was 20%, and after the destruction of the worm the eosinophiles fell to 8% in the course of a few weeks. The examination of the blood in one case of bothriocephalus latus showed no increase in the eosinophilic cells although the stools contained a large number of Charcot-Leyden crystals which are usually seen in connection with eosiniphilia. In all cases of asthma in which I have had occasion to examine the blood, the eosinophilic count has been high, usually about 20%.

Dr. Janeway: Last year I observed moderate eosinophilia, 5 or 6%, in some cases of vaccinia, but subsequent study made upon a number of other cases convinced me that this was not a constant finding.

Dr. Conner: In a case of severe secondary anæmia dependent upon the presence within the intestine of anchylostoma duodenalis, I observed an eosinophilia of eight to twelve per cent.

Dr. Lartigau: I have been particularly impressed with the frequency with which eosinophilic cells may be found in serious membrane exudates. During the last six months, Dr. Moschowitz has regularly made examinations of such exudates and transudates in Roosevelt Hospital and in a certain proportion of the cases, particularly the pleuritic ones, a very striking eosinophilia was noted. In one case in particular, the cells were almost exclusively of this type; but in this case the etiology of the pleurisy could not be established. A differential diagnosis of the blood showed a slight increase in the percentage of eosinophiles, but it was by no means proportionate to the number of these cells in the pleural exudates.

Dr. Wightman: It seems to me that one should closely hold in mind the personal equation feature in blood counting. To my mind this accounts for a good many of the differences reported by different observers. This applies especially to the count of eosiniphiles and polymorphonuclear cells. I used the methylene blue and eosin stain as a control to the tri-acid stain in my studies.

A CASE OF CUTANEOUS PIGMENTATION WITH LESIONS IN THE ADRENAL GLANDS.

HARLOW BROOKS, M.D.

The case which is the subject of this report was a woman, forty-five years of age. The previous history could not be obtained because of the mental state of the patient at the time of her admission to Bellevue Hospital The physical examination showed that she was a poorly nourished woman, with marked œdema of the extremities and darkly pigmented areas over the entire trunk and thighs. On admission, the patient was almost in a state of collapse, the pulse being small, rapid and weak. The lungs seemed normal and the liver extended two fingers breadth below the free border of the ribs. On the day after admission the temperature rose and evidences of pneumonia was observed. From the results of the urine examination, a diagnosis of chronic interstitial nephritis was made. The examination of the blood showed evidence of marked primary anæmia. The patient died.

The autopsy could not be obtained until the day after death, consequently no histological examination was made. The pigmented areas in the skin involved the trunk of the body, and both arms as far as the middle third of the forearm, and the greater portion of both thighs. The backs of the hands were also slightly pigmented. Further, the skin showed many scars, the result of bites of parasites. These scars when they appeared on the pigmented areas were distinctly white. The skeletal muscles were light brown in color and very soft. An obliterative subacute pericarditis was present and the left pleural cavity was obliterated. The myocardium was soft and light in color. The subcutaneous fat and that over the heart was of a very peculiar color, resembling lard. The thyroid gland was noticeably small though apparently normal in structure. The glands of the neck were deeply pigmented black; the left lower lobe of the lung showed well marked monoconsolidation and miliary tuberculosis. The liver was enlarged and fatty. No definite lesion was observed in the pancreas, nor was any noteworthy observed in the gastro intestinal canal. The left kidney presented the characteristic appearance of a large "white kidney". The right kidney,

on the other hand, was very small and its parenchyme was largely replaced by fibrous tissue which appeared to contain old tuberculosis. Both adrenals presented a peculiar pink cortex associated in the left kidney with fatty areas. On microscopical examination the peripheral lymph nodes showed no differentiation between the cortex and medulla. There was an infiltration of the cells whose nuclei showed more or less degeneration. Sections of the peculiar fatty tissue in the left adrenal presented no noteworthy microscopical appearances. In the involuntary muscles most of the fibres were small, but here and there swollen and degnerated ones were observed. The heart muscle showed considerable infiltration with fat, but no pigment deposition in the muscle fibres.

Here and there small areas of round cell infiltration were observed in the myocardium. Microscopical lesions of the stomach pointed to a chronic atrophic gastritis, and those of the liver to fatty infiltration. The left kidney showed acute parenchymatous nephritis with extensive fatty degeneration of the epithelium. Sections of the right kidney showed that the fibrous process was of a tuberculous nature. Numerous sections of the adrenal glands showed similar lesions on both sides. The capsules were not thickened, but there was a general and well marked increase of the connective tissue frame work. Individual fibrilla were swollen and œdematous. The blood vessels were moderately congested with occasional extravasations of the blood. As a rule, the acini were made up of normal cells, and such changes as were found involved the whole acinous. Extensive fatty degeneration wa present in both the medulla and cortex. There were pigmentary depositions within the glands. In the medulla and throughout other portions of the gland there were found cells which were two or three times larger than normal. Other cells with large chromatic nuclei were present in groups. Around some of the blood vessels small œdematous masses were found.

In Addison's disease, the pigmentation is usually found in the more exposed parts of the body, while in this case these areas were the least pigmented. It seems probable that if the subjective history of the patient could have been obtained that this would have been one similiar to that given by cases of Addison's disease. The lesions of the viscera correspond rather closely with those met with in Addison's disease, although it should be remembered that exposure and the destitute state of the patient were sufficient to explain the lesions observed. It is a well-known fact that tuberculosis of the adrenal gland may occur without the development of symptoms of Addison's disease. I reported such a case to this Society some years ago. In summing up the evidence it seemed to me that the case cannot be looked upon as one of Addison's disease, but may be considered as an example of "vagabond's disease" with secondary disease of the adrenals.

Discussion.

Dr. Janeway: I quite agree with Dr. Brooks in not considering this case Addison's disease, inasmuch as the clinical picture certainly lacks some important features. The absence of pigmentation of mucous membranes and exposed portions of the body further strengthens this view. Moreover, the extreme anaemia observed in this case is by no means characteristic of Addison's disease. In two cases of this disease which I saw shortly before death the anaemia had not been marked. A review of the literature shows that marked anaemia is evidently not a conspicuous feature of the clinical picture.

Dr. Libman: In one case of Addison's disease which I saw two years ago, there was evidence of anaemia. An autopsy was made in this case and the post-mortem examination showed tuberculosis of the adrenal glands. In another case which was not autopsied there was the usual pigmentation and the blood picture was that of pernicious anaemia.

Dr. Connor: Does Dr. Brooks look upon the changes observed in the adrenals in his case as very uncommon? If there had been no pigmentation of the skin would the changes in the adrenals have led him to suspect anything abnormal? I ask this question because of the great variations often observed in adrenals which are apparently normal.

Dr. Coleman: From an extensive study of the adrenal glands, I have been much impressed with the difficulty of telling much about the finer changes in this organ unless it is obtained shortly after death and carefully hardened. On gross examination in many of these cases which I studied the whole medulla and a portion of the cortex were converted into what seemed colloid material. If the hardening be in alcohol or formalin this can not be made out by microscopical examination. Personally I am not disposed to look upon the changes in Dr. Brooks' case as the cause of the pigmentation of the skin. One of the cases of Addison's disease which I was able to study post-mortem was a patient who had been sent to Bellevue Hospital from the Chambers Street Hospital with a diagnosis of chronic constipation, and although under observation for several weeks at Bellevue Hospital, there seemed to be no reason to change this diagnosis. At the autopsy both adrenals were found completely destroyed by tuberculous process. One of them was considerably larger than normal, and the other only slightly increased in size. The smaller one was calcareous while the other was caseous. Neither adrenal showed any trace of adrenal tissue. In this case there was no pigmentation of the skin whatsoever. I am disposed to look upon the pigmentation in Addison's disease as the result of some lesion of the ganglia of the sympathetic system. Duhring has shown that a lesion of the sympathetic ganglia may be followed by

pigmentation without the usual symptoms of Addison's disease. The cases of "vagabondism" which I have seen showed distribution of the pigment almost identical with that found in Dr. Brooks' case. The malnutrition and the previous depressing influences of the tuberculosis seem to me quite sufficient to explain the skin pigmentation in the case just reported.

Dr. Philips: With the exception of pigmentation, the case reported by Dr. Brooks certainly presented no symptoms of Addison's disease. Artefacts in the adrenal glands are very common occurrences. Some of the changes described by Dr. Brooks are undoubtedly pathological, especially the changes about the blood vessels and the connective tissue increase and atrophy and disappearance of the glomeruli. The chromatin changes and the change in the fat content may easily be confounded with changes met with in the normal gland.

Dr. J. Levene: Dr. Brooks' case is highly interesting in suggesting the doubt of any relationship between pigmentation of the skin and disease of the adrenal glands. I am not inclined to look upon the case as one of Addison's disease.

Dr. Brooks: The pigmentation of the skin was marked and covered the whole trunk, a symptom very different from that generally observed in "vagabond's disease". In answer to Dr. Connor's question, I may say that I believe the lesions of the adrenal glands would have been sufficient to attract my attention, even if the skin pigmentation had been absent. Like some of the other members of the Society, I have been impressed with the artefacts in the adrenals; but allowing for this source of error, it seems to me that the presence of cell mitosis and giant cells containing a typical nitoses is sufficient to consider these changes as evidences of pathological conditions.

PRIMARY PIGMENTED SARCOMA OF THE FOURTH VENTRICLE OF THE BRAIN.

J. H. Larkin, M.D.

This tumor was removed from a male, 46 years of age. There was a history of paralysis of the external rectus and abducens muscles, with facial atrophy of the left side. There was no headache or vomiting at first, and no evidences of brain tumor at the start. Later, the paralysis became well defined and examination of the fundus showed marked choked disc. For three months the patient attended to his routine duties, although he occasionally fell in the street and temporarily lost consciousness. Finally, the

vertigo became so pronounced that he was compelled to remain at home. He eventually died of pneumonia.

At the autopsy two tumors were found,—one a psammoma of the pineal gland, and the other a pigmented tumor on the floor of the fourth ventricle in the region of the anterior fovea. A large and engorged vein was also observed on the floor of the fourth ventricle.

Sections of the tumor examined microscopically showed extreme cellular growth composed of polyhedral cells and stroma with many new-formed blood vessels. The periphery of the tumor contained considerable blood pigment, while the central parts contained melanotic pigment.

MESENTERIC ABCESSES WITH SECONDARY THROMBOSIS OF THE MESENTERIC AND PORTAL VEINS.

E. LIEMAN, M.D.

In forty-eight cases of appendicitis, I have found suppurative lesions of the mesenteric and portal veins in six. In four of the cases, there were multiple abscesses of the liver. The liver in one case appeared on gross examination to be merely dry; but histological examination showed that there was pus between the liver cells. The specimen which I have presented is one showing multiple abscesses of the mesenteric veins with purulent thrombosis of the mesenteric and portal veins. The subject was a patient who had been admitted to Mt. Sinai Hospital with a diagnosis of appendicitis. He had two chills just prior to his admission. At the operation there was a suppurating appendix and mesenteric abscess. The patient did not do well after the operation, and although other abscesses were suspected and searched for, no effectual treatment along this line could be carried out. Cultures from the abscesses contained streptococci.

A search through the literature shows that this complication in appendicitis has been met with by me about twice as frequently as in the reported experiences of others. This may be explained by the fact that most of the reported cases occurred before the days of frequent operations for appendicitis. Ordinarily, a case of suppurating thrombosis of the portal vein with multiple abscesses is looked upon as fatal.

Discussion.

DR. WOOD: In those cases of mesenteric and portal vein thrombosis which have gotten well, the infection may have been with a colon bacillus of low virulence, such as is seen in cases of biliary cirrhosis. The invasion of the colon bacillus in the cir-

rhosis cases usually induces only small areas of necrosis and pus formation which may be followed by recovery.

DR. LIBMAN: In the case I have reported the abscesses showed evidence of healing, and the infection was due to the streptococcus. The infection at first seemed quite virulent. The lesions in the portal vein and liver showed almost complete organism, the fatal issue having been due to a large abscess in the mesentery as may be seen in the specimen which I have presented.

DERMOID CYST OF THE OVARY WITH CARCINOMATOUS CHANGES.

F. C. WOOD, M.D.

This specimen was taken from a woman, fifty years of age, who gave a history of indefinite symptoms of pelvic origin. The clinical diagnosis was that of some acute infection of the pelvis. On opening the abdomen, there was found a thin-walled cyst containing the usual amount of fat, but without the usual accompaniment of fat. The usual rudiments of the embryo found in these dermoid tumors were not discovered in this specimen. The rudimentary head of the dermoid was rough and presented a peculiar appearance. On section it had the characteristic appearance of an epithelioma. The pearls were not very well formed and there were not many giant cells. These cells probably arise from insufficient nuclear division, and may be explained by the presence of hair which acted as a foreign body, giving rise to foreign body giant cells. A search through the literature shows that only sixteen authentic cases of this kind have thus far been reported, although there are a number of imperfect reports without accurate microscopical examinations. One case has been described in which there was a rudimentary mamma in the dermoid and from it was growing a rudimentary carcinoma.

MULTILOCULAR ECHINOCOCCUS CYSTS OF THE LIVER.

I. T. LEWALD M.D.

The specimen subject of this report was presented at the last meeting as a case of primary carcinoma of the liver. Further microscopical examinations have convinced me that there is not sufficient evidence upon which to base such a diagnosis. There was a slight alveolar arrangement but no true epithelial cells were

found, although many small round cells and areas of degeneration were present. At the suggestion of Drs. Oertel and Dunham, a more careful examination has been made of different parts of the new growth. The results of such study have convinced me that the lesion is one of multilocular echinococcus cysts of the liver. Three cases of this kind have been reported in this country; one by Prudden, in 1883; one by Gardner Dean, in 1887; and one by Oertel, in 1899. In all of these cases and in the present one, the growths occurred in foreign-born individuals. The symptoms have been strikingly similar in all cases. In Prudden's case, a diagnosis of hepatic abscess had been made; while in Oertel's case, a provisionary diagnosis of echinococcus cysts was made before operation.

In the specimen which I presented the entire left lobe is occupied by new growth which shows evidence of peripheral extension. It is broken down in the centre, whilst the peripheral parts are made up of dense fibrous tissue. On close examination I discovered a number of small translucent areas which on microscopic examination were shown to be small cysts.

Index to Volume I, New Series.

PAGE

Abscess—Mesenteric 140
Adrenal—Lesions of 136
Aneurysm—Aortic 35
" 100
" 118
" 130
" Basilar 16
" Cerebral 16
Aorta—Aneurysm of 35
" " 100
" " 118
" " 130
Apparatus—Anærobic cultures 115
Appendix—Tuberculous 17
Bacillus Aerogenes Capsolatus 1
Basilar Artery—Aneurysm of 16
Biggs—Phlegmonous gastritis 125
Syphilitic bronchial stenosis 129
Blood—Differential count 134
Blumer—Bacteriology of pneumonia 21
Boldt—Salpingitis 36
Bolduan—Pernicious malaria 134
Breast—Endotheliona of 14
Bronchi—Syphilis of 129
Brooks—Adrenal lesions 136
Bacillus ærogenes capsulatus 1
Miescherschen Schläuche 116
Carcinoma—in dermoid 141
of kidney 117
" liver 32
" peritoneum 11
Cerebral Artery—Aneurysm of 16
Coleman—Aortic aneuysm 100
" " 118
Human glanders 108
Coma—Experimental 112
Cordes—Duodenal occlusions 70

PAGE
Cyst—Dermoid 141
Echinococcus 141
Renal 15
" 17
Dermatitis—Exfoliativa 126
Diazo-reaction—in phthisis 80
Diphtheria bacillus—Morphology of 93
Dow—Aortic aneurysm 130
Dunham—Anærobic apparatus 115
Duodenum—Occlusions of 70
Endocarditis—Gonorrhœal 97
Pneumococcic 80
Endothelioma—Mammary 14
Peritoneal 80
Ewing—Human glanders 103
Peritoneal carcinoma 11
Fat-necrosis—Appearences simulating 117
Gastritis—Phlegmonous 108
" 125
Glanders—Human 103
" 120
Goldhorn—Stain for plasmodium malariæ 7
Herter—Experimental coma 112
Iso-agglutination 123
Hodenpyl—Mammary endothelioma 14
Renal cyst 15
Holder—New animal 132
Iso-agglutination 123
Janeway—Lymphatic leukæmia 33
Kidney—Cyst of 15
" 17
Larkin—Sarcoma of brain 139
Stenosis of pylorus 79
Lartigau—Thyroidal sarcoma 85
Larynx—Syphilis of 97
Leukæmia—Lymphatic 33
Libman—Mesenteric abscesses 140
Proteid precipitation 83
Liver—Carcinoma of 32
Lewald—Cystic kidney 17
Ecchinococcus cyst 141
Laryngeal syphilis 97
Myomatous uteri 18
Pernicious malaria 119
Pulmonary thrombosis 133
Stomach, malforation of 120
Malaria—Pernicious 119
" 134
Stain for parasites 7
" " 95

PAGE
Miescherschen Schlauche 116
Minot—Middleton Goldsmith Lecture 39
Morphology—of diphtheria bacillus 93
Park—Experimental tuberculosis in calves 111
Pathology—Embryological basis of 39
Peritoneum—Carcinoma of 11
Endothelioma of 80
Pneumonia—Bacteriology of 21
Potter—Human glanders 120
Prostate—Hypertrophy of 18
Proteids—Precipitation of bacteria 83
Pylorus—Stenosis of 79
Salpingitis—Gonorrhœal 36
Sarcoma—Cerebral 139
" Thyroidal 85
Schlapp—Intramedullary degenerations 113
Schultze—Aortic aneurysm 35
Basilar " 16
Cerebral aneurysm 16
Fat-necrosis 117
Gastritis 108
Thrombosis of vena cava 76
Technique—of frozen sections 110
Thayer—Atresia of duodenal papilla 127
Carcinoma of liver 32
" " stomach 133
Dermatitis exfoliativa 126
Hypertrophied prostate 18
Thrombosis—of portal vein 140
of pulmonary artery 133
of vena cava 76
Thyroid—Sarcoma of 85
Tuberculosis—of appendix 17
of urinary organs 36
Uterus—Myomata and pregnancy 18
Vena Cava—Thrombosis of 76
Wightman—Blood Studies 134
Williams—Morphology of diphtheria bacillus 93
Wilson—Animal holder 132
Gonorrhoral endocarditis 97
Wood—Dermoid cyst with carcinomatous changes 141
Diazo-reaction in phthisis 80
Endocarditis-pneumococcic 80
Endothelioma of peritoneum 80
Technique of frozen sections 110
Stains for malarial organisms 95

RB
1
N32
n.s.
v.1

New York Pathological
Society
Proceedings

Biological
& Medical
Serials

PLEASE DO NOT REMOVE
CARDS OR SLIPS FROM THIS POCKET

UNIVERSITY OF TORONTO LIBRARY